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Original Communications

BIO-ELECTRIC CORRELATES OF THE MENSTRUAL CYCLE IN WOMEN*

H. S. BURR, PH.D., AND L. K. MUSSELMAN, M.D., NEW HAVEN, CONN.

(From the Departments of Neuro-Anatomy and Obstetrics and Gynecology, Yale School of Medicine)

THE PROBLEM

RECENTLY there have appeared two reviews of the literature dealing with the time of ovulation in women (Knaus 1929, Hartman 1936). From these it is evident that a wide variety of techniques have been used in the analysis of this problem. The methods employed have ranged all the way from a determination of the time of the greatest sex desire to the observation of the ovaries at laparotomy. Inasmuch as direct studies of the human female have given suggestive but not conclusive evidence, numerous observers have sought the answer in studies of ovulation in infrahuman mammals.

Of the various lines of approach, much has been made of the examination of the corpus luteum at the time of operation. The majority of gynecologists present evidence to show that records of the age of the corpus luteum indicate that ovulation occurs between the fourteenth and sixteenth days of the menstrual cycle. Novak (1934) and others are of the opinion that it is impossible to correctly estimate the age of the mature corpus luteum even from histologic examination.

Since the development of the corpus luteum is believed to be due primarily to the hormone activity of the anterior lobe of the pituitary gland, it might be assumed that tests of the blood and urine for this

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hormone would be of value. Thus far the tests reveal the blood level of the hormone to be at its peak in the last part of the cycle while the level of the hormone in the urine is highest in the middle of the cycle. Obviously these findings tend to confuse the problem. From experiments on the motility of the human uterine musculature in the presence of the corpus luteum hormone and its reaction to pituitrin, on the various days of the cycle, Knaus (1929) concluded that physiologic ovulation occurred fifteen days before the ensuing period in women with normal reproductive physiology. Unfortunately, his results are not substantiated by most of the other investigators.

According to Papanicolaou (1933), studies on the changes in the vaginal epithelium reveal that in one-third of women near the time of ovulation vaginal smears show large and characteristic cells with a marked decrease or absence of leucocytes and often an increase in the amount of mucus. At the time of ovulation there is a decrease in the mucus with an increase in the number of leucocytes and a scaly type of cell, sometimes accompanied with red blood cells. From these observations Papanicolaou believes that ovulation occurs frequently on the twelfth and thirteenth days.

As a result of his examination of the endometrium in 898 cases, Schroeder (1928) concluded that ovulation occurred upon the fourteenth to sixteenth day of the cycle. This study, based upon microscopic examination of the endometrium which was correlated with the menstrual data of patients who had a twenty-eight-day cycle, has been questioned by some; for in the first place the patients' memories may have been unreliable and second, the entire endometrium was not always available for study.

TABLE I. NUMBER OF DAYS INTERVENING BETWEEN MENSES

SUBJECT	OWN ESTIMATE OF INTERVAL DAYS	ACTUAL INTERVAL				
		1	2	3	4	5
1	21-24	26	24	24	27	–
2	28-34	28	24	27	31	32
3	28	29	25	28	28	–
4	28	30	27	28	28	–
5	38-46	50	33	31	–	–
6	26	26	24	26	22	25
7	30	32	35	32	30	–
8	28	30	35	29	31	–
9	28	26	30	28	28	27
10	28-30	Pregnant				
11	23-27	30	22	–	–	–
12	28-32	29	31	25	27	–

A similar objection is raised to the simple biopsy method, since sections taken in the same patient from different areas of the endometrium often present variable histologic pictures. Observations based upon instances of isolated coitus followed by pregnancy and cases of success-

ful artificial insemination suggest that ovulation occurs most frequently at the middle of the menstrual cycle.

Newell, Allen, Pratt and Bland (1930) recovered five unfertilized human ova from the Fallopian tubes at operation, and concluded that ovulation in these instances had occurred a day or two before the fourteenth day of the cycle. Attempts to deduce the time of ovulation from a study of embryos and the dates of menstruation are thus far of little value and, because of the lack of accurate information, unsatisfactory. It is clear that the weight of evidence suggests that ovulation in women occurs during the middle of the menstrual period, and similar investigations in monkeys seem to confirm this.

From a study of ova recovered at laparotomy, Corner and Allen (1929) concluded that ovulation took place between the eleventh and fourteenth days of the cycle. By rectal palpation, Hartman decided that ovulation takes place in the monkey on the average between the twelfth and thirteenth days, while the range is from nine to eighteen days. By the vaginal smear method, Davis and Hartman (1935) found that while the exact time of ovulation could not be determined, it never occurred in the late premenstruum but usually about the middle of the cycle. In analyzing 52 pregnancies which resulted following 420 copulations on various days of the cycle in monkeys, Hartman (1936) found that 49 occurred from coitus on the eleventh to the sixteenth days inclusive of the menstrual cycle.

Inasmuch as Burr, Hill and Allen (1935) were able to show marked rises in potential difference associated with ovulation in the rabbit, it was suggested that the rise in potential difference in the human female might also be associated with ovulation.

Recently we (1936) observed marked variations in the bio-electric potential difference between the index fingers of the two hands in the human female which correlated with the evidence of the menstrual cycle. They reported that normally the right index finger was several hundreds of microvolts positive with respect to the left. During the menstrual flow, however, this voltage difference decreased significantly and on occasions showed a positive potential in the left index finger. In addition, between the fourteenth and seventeenth days preceding the onset of the subsequent menses, the right index finger showed an increase in positive polarity amounting to several thousands of microvolts. For nine successive months, the electrical cycle repeated itself with astonishing accuracy. Similar records from a pregnant female showed an entire absence of such monthly cyclic phenomena. In order to extend these observations on a larger scale, finger to finger tests were made on fourteen women for three successive months. Of these, one was in the period of normal menopause, one artificial menopause following a panhysterectomy with bilateral salpingo-oophorectomy, 8 were single, 3 married, and 1 married and pregnant.

THE TECHNIQUE

The procedure employed was exactly like that described by us (1936). As nearly as possible, daily determinations were made on each individual with the exception of Sundays, holidays, and vacations. The index finger of each hand was placed in a beaker of physiologic salt solution which was in direct contact with the salt solution of the electrode chambers through glass tubing. Five successive determinations were made at each sitting, the fingers being removed from the salt solution between each reading. The values obtained were averaged for each day, and graphs prepared for each individual. Results strikingly similar to those previously reported were found with certain highly interesting differences. Attention should be called to the fact that there is no direct explanation of the mechanism involved in the production of changing bio-electric potentials which seem to correlate with the menstrual cycle. Nevertheless, it must be borne in mind that the technique used was developed in order to study more rigorously the possible presence of an electro-dynamic field in all living systems (Burr 1932; Burr and Northrop 1935; and Northrop and Burr 1937). A considerable number of studies attest the presence of such a field, and it seems not unlikely that some of the properties of this field of the organism correlate with such fundamental physiologic processes as the menstrual cycle.

RESULTS

Consideration of the data reveals that the determinations are made at the index fingers, a considerable distance from the major physiologic activities associated with menstruation. The correlations which have been noted are astonishing, and no ready explanation is at hand for the obvious "action at a distance." However, two possibilities may be considered. The presence of negative currents of injury has long been noted by physiologists, and since the menstrual flow is associated with the breakdown of tissue it might, therefore, be expected to show such currents. Yet the data demonstrate that the period of the menses is a period of low voltage difference between the two index fingers. Moreover, the peaks of potential difference to be seen in the intermenstrual period seem unrelated to any extensive injury of the genital tract, although it cannot be denied that the rupture of the egg from the follicle is associated with a minimum amount of injury.

However, the ovulation studies of Burr, Hill and Allen (1935) show that the voltage rise between the symphysis and the vagina in the rabbit develops parallel with the increase in size of the follicles, with a rapid return to the base line after the egg leaves the follicle. It is difficult to see, therefore, how negative currents of injury could explain the phenomena, nor does any immediate explanation arise from the fact that the activity in the pelvis is reflected in the finger tips. If, however, it

is assumed that the living organism possesses an electrodynamic field, such profound physiologic rhythms as are associated with the menstrual cycle might be expected so to modify the entire field that evidences of local activity could be detected anywhere throughout that field. At present no experimentally demonstrated set of facts is available to explain the origin and propagation of these bio-electric potentials. A great deal of careful analytical work will be required before this question can be answered. The data collected are presented in graphic form in Figs.

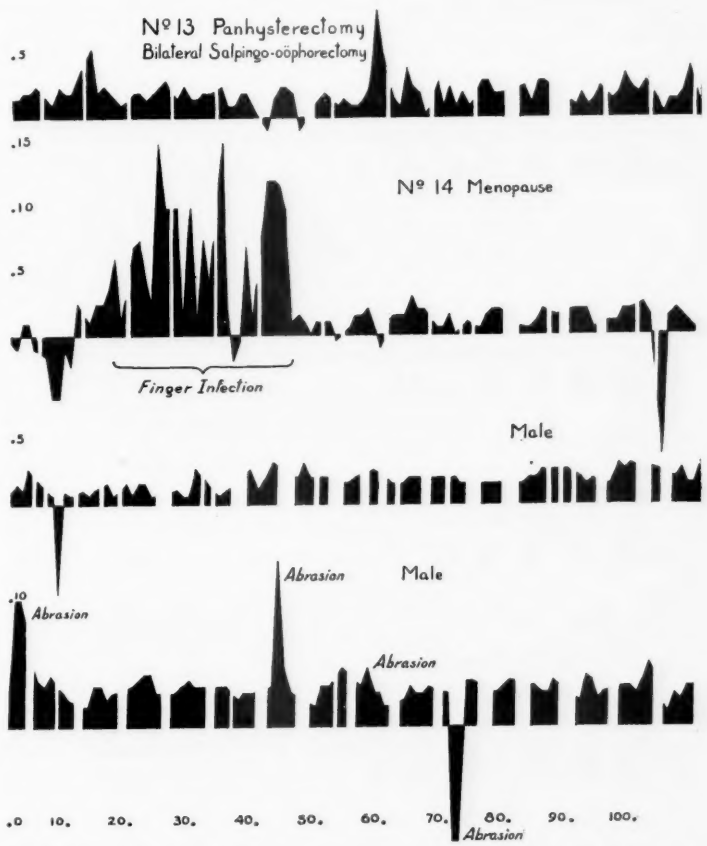

Fig. 1.—Plots of voltage difference in two males and two females in millivolts against successive days. Note effect of extraneous factors such as abrasions and skin infections.

1 to 4. It will be seen at once that this pattern is a highly variable one, not always consistent with the same individual.

The four graphs in Fig. 1 are from two males and two females. One of the females was in the menopause and the other had a panhysterectomy. The two males showed no cyclic phenomena whatever and in the second instance in particular, the only marked voltage differences detected were those which were associated with minor abrasions, cuts, or hangnails on the fingers being tested. A similar irregularity is to be seen in the individual with the normal menopause in whose left index finger

there was a ringworm infection treated by x-ray. In the case of the panhysterectomy, there are two elevations of voltage difference for which no correlate could be determined.

In Fig. 2 are to be seen graphs of those individuals in which a marked rise in the potential differences was found in and around the middle of the menstrual period. In Patient 1, in four months, only one genuine peak was recorded but it will be noted that this patient was absent on corresponding days of each of the three other cycles. Patient 2 was difficult to classify in that during the second and third

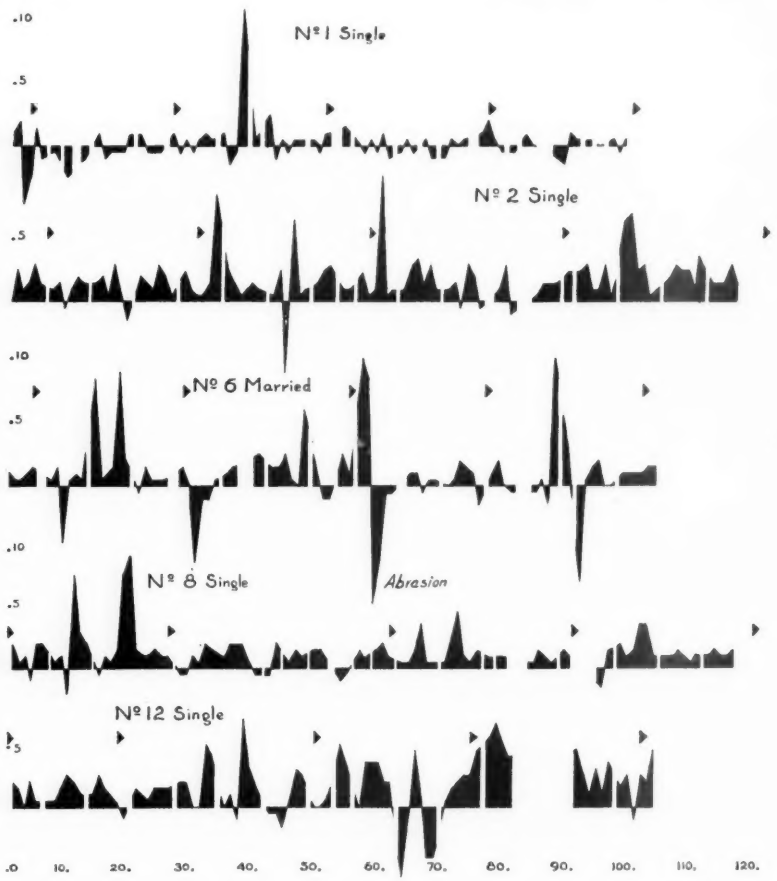

Fig. 2.—Similar graphs from individuals showing marked rises in potential in and around the middle of the period.

months peaks occurred right after the menses; whereas in the fourth month it occurred about the middle of the period. In Patient 6 peaks occurred in the middle of the cycle during the first and the last month but during the third period a peak showed immediately following menstruation. Patient 8 showed two high peaks in the first period, none in the second and no peaks in the third and fourth periods. Patient 12 was difficult to classify since there seemed to be little regularity.

In Fig. 3 are graphs from patients showing the greatest electrical differences in the few days immediately following menstruation. Patient 7 showed the greatest irregularity of any of those studied. A peak was observed at the end of the first

month under observation, during the first third and last third of the second and third months, and for the fourth month the readings were complicated by injury to the index finger of the right hand. In the first month, Patient 9 gave readings complicated by a traumatized finger in the left hand but in the second and fourth months showed moderate peaks immediately after the menses with no irregularity in the third month, due probably to failure in obtaining regular readings. Patient 11

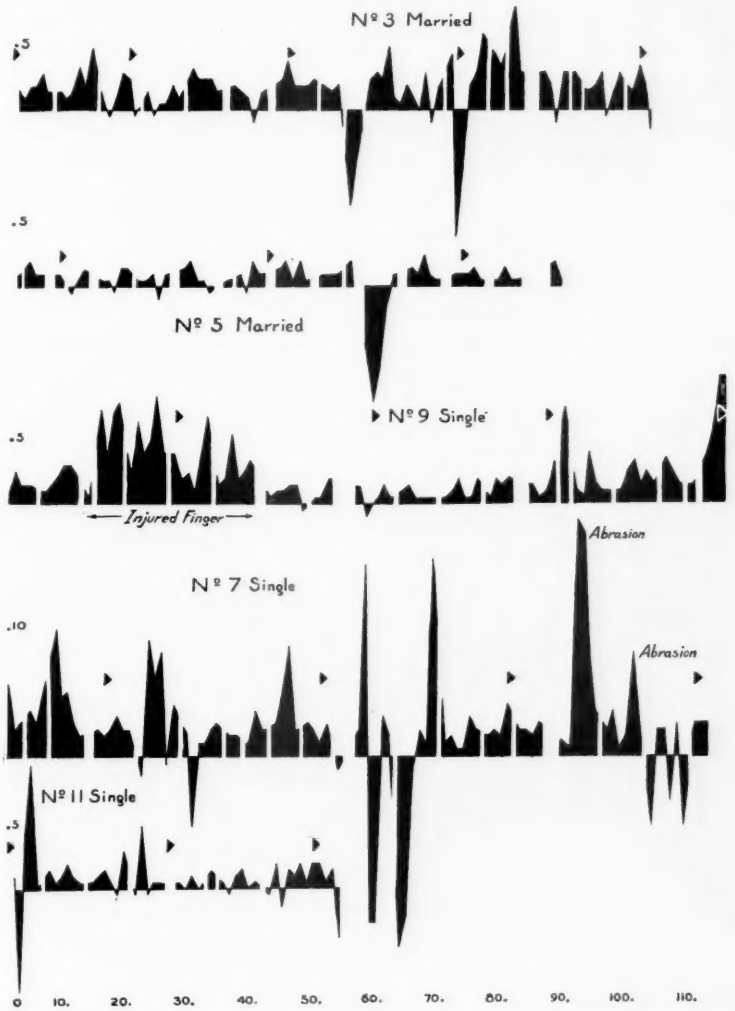

Fig. 3.—Graph showing rises in potential difference chiefly during the few days following menstruation.

showed a marked rise immediately after menses in the first month but none in the second. Patient 3 showed such irregularity as to make classification difficult, as during the third month there was a marked rise at the middle of the period but with a polarity which was reversed with respect to the usual determinations. Patient 5 shows a fairly stable baseline except for the middle of the second period when a marked voltage difference of reversed polarity was observed.

Fig. 4 shows the two patients with marked differences from any of the others. Patient 11 would seem to be completely anovulatory if the rise in voltage difference observed is to be correlated with ovulation. In any event, no significant voltage shifts were observed. Patient 10 is particularly interesting because of pregnancy. A comparison of this curve with that derived from another pregnancy (Burr and Musselman, 1936, Fig. 2) shows an astonishing similarity. The three deviations from the baseline in both patients occurred at approximately the same time in pregnancy and the voltage shifts were in the same direction. Correlates for these deviations are entirely unknown.

The above data can be examined from a somewhat different angle. In the group under observation, Patients 1, 2, 4, 7, 8, 9, 11, and 12 were single. Patients 3, 5, and 6 were married and Patient 10 was married and pregnant. The graphs of the married women, Numbers 3 and 6, show signs of greater bio-electric activity than was to be seen in any of the single women except Patient 7. If it should turn out that these peaks are genuinely associated with ovulation, these data suggest a possible correlation between coitus and ovulation.

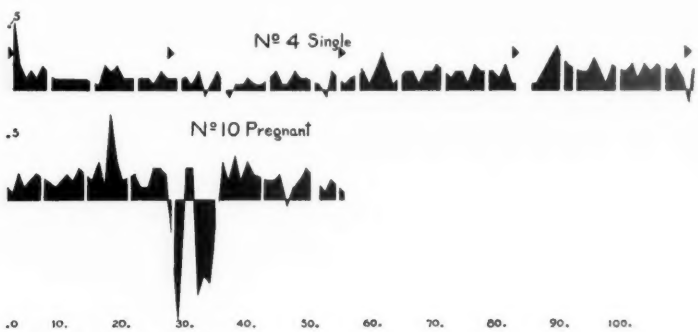

Fig. 4.—Two graphs, one from an apparently anovulatory subject and the other during the middle of pregnancy.

It will be noted further that the graphs present suggestive evidence that certain subjects are completely anovulatory. For example, in Patient 4, the times of the peaks in the cycle are not always consistent. In contrast to the previous study (Burr and Musselman, 1936) where the peaks occurred with astonishing regularity in the middle of the period, the present data show that such regularity is not always present. The graph of Patient 1 is probable evidence of a regular cycle although lack of readings in the first, third, and fourth month at the proper time makes a definite decision impossible. Patient 2 is interesting because the second and third months show peaks immediately after the menstrual period, whereas the last month shows one approximately in the middle. Patient 6 shows two months with peaks in the middle and one with the peak immediately after the period. The graph of Patient 9, which is complicated by an injury to the left hand, shows peaks in the second and fourth months but none in the third which may have been a result of absence. Graph 11 in Fig. 3 shows a peak immediately after the

period in the first month, a much lower peak at the end of that same period and no peaks in the following period.

While it is possible that ovulation may occur at any time, yet it is highly probable that there are periods entirely without ovulation. Should it eventually develop that the marked bio-electric rises in the voltage difference between the two fingers were correlated with the time of ovulation, the data here presented would indicate that the rupture of the follicle occurs most commonly either in the middle of the cycle or immediately after menstruation. There are no unequivocal cases of peaks immediately preceding menstruation. Furthermore, the data seem to indicate that the cycle is by no means constant in the same individual. Studies are now being undertaken which combine other techniques for the determination of ovulation, and which extend over longer periods of time in the hope that more definite results may be obtained.

Since the above data were collected Burr, Musselman, Barton and Kelly (Science 86: 312, 1937) have succeeded in obtaining a continuous graph of the changes in bio-electric potential associated with ovulation in a human being. With one electrode in the vagina and one on the symphysis the record shows a swing of the vaginal potential from a base line of –20 millivolts to +30 millivolts. About twelve hours later, this potential difference increased suddenly, without warning, to about +100 millivolts, throwing the recording mechanism off scale. In fifteen minutes an abrupt drop to 70 millivolts occurred. This was followed fifteen minutes later by another drop to 30 millivolts. At laparotomy, fourteen hours later, the punctate hemorrhage of a ruptured follicle was observed and the corpus luteum excised. Microscopic examination shows a well marked corpus hemorrhagicum and a clearly defined corpus luteum. This observation gives weight to the bio-electric data described above, since it indicates that in a human being, as in the rabbit, ovulation is accompanied by voltage surges of considerable magnitude.

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DURATION OF SECRETORY ACTIVITY IN THE GLANDS OF THE DECIDUA VERA*

SOMERS H. STURGIS, M.D., BOSTON, MASS.

(From the Ovarian Dysfunction Clinic of the Massachusetts General Hospital)

WHEN an ovarian cyst is discovered in pregnancy, the question of operation generally arises, and if on exploration the tumor is found to involve the corpus luteum, the surgeon must then weigh the consequences of its excision. It is known that the corpus luteum is essential for implantation, but it has not been definitely established how soon after conception this organ may invariably be dispensed with, in the human being, without interrupting the course of gestation. It was in dealing with this problem that the following study of secretory activity in the glands of the decidua vera was suggested. It was thought that the duration of the response of these glands to the luteal hormone might indicate the period during which progestin could be considered a physiologic necessity to the life of the fetus.

The possibility of having to remove the corpus luteum occurs whenever a tumor of the adnexa complicates pregnancy. This is not by any means a rarity. From admissions to the Sloane Hospital for Women in New York, Caverly[1] has recorded the incidence of this complication in over 16,000 pregnancies to be 1:500. He reported torsion, hemorrhage, or other acute conditions associated with the cyst itself in 25 per cent of this group and, therefore, advised operation in all cases.

But when a pathologic tumor of the ovary is palpated early in gestation, and when there are no symptoms referable to it, the decision to operate may well depend on evidence indicating when the corpus luteum could, if necessary, be safely excised without risking miscarriage or abortion. Such evidence may be derived from three sources: first, from case reports of successful excision in the literature; second, by analogy from animal experiments, and third, from biologic tests for the presence or absence of the luteal hormone at difference stages of pregnancy.

In a review of the literature ten years ago, Ask-Upmark[2] collected 50 cases of removal of the corpus luteum within the first two months, and of these patients, 33 per cent miscarried. Asdell[3] in 1928 reported 38 cases, four of which miscarried. In Caverly's series of 83 cases of ovarian tumor excised during pregnancy, six of the specimens contained the corpus luteum; of these, only the earliest gestation

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at two months was interrupted. We have recently seen three cases in this hospital;* in two, the operation was done eight weeks after the last menses, and they both miscarried on the fifth and ninth day postoperatively. The third pregnancy, one of ten weeks, was not disturbed by removal of a large lutein cyst. There are numerous reports of isolated cases of this procedure scattered through the recent literature, but interpretation of this evidence is difficult. It has been pointed out[3] that most of the cases have been recorded simply because a viable baby was obtained in spite of unilateral or bilateral oophorectomy, yet it is probable that a great many similar operations resulting in miscarriage never have appeared in print. Many of the authors do not always explicitly state that a retained ovary was even visualized, and it is impossible to be certain that all luteal tissue has been removed in such reports. The factor of trauma incident to the operation varies widely in the hands of individual surgeons, yet may at times play a part in subsequent miscarriage. Unfortunately, there has never been, and probably never will be, a large series of consecutive cases of removal of the corpus luteum in different stages of gestation, carefully controlled and reported in detail by one man; the reason is obvious. The case reports that are available merely suggest that after the second month the corpus luteum may often, but not always, be removed without interrupting pregnancy, whereas before the second month such an operation seems to result in from 10 per cent to 33 per cent of miscarriages. More definite conclusions are hardly justified because of the above considerations from the data in the literature alone.

Animal experimentation has demonstrated a species variability in the dependence of successful gestation on the corpus luteum. Thus, the goat and opossum, squirrel, mouse, and bitch[4] will almost invariably miscarry after double ovariectomy at any stage of pregnancy. The rabbit will always miscarry if operated upon within eight days of mating, and generally at any subsequent time before term.[5, 6] The guinea pig, however, will generally carry through such a procedure without interruption, if it is done more than two days after conception.[7] But the results of these investigations cannot reasonably be applied to the same problem in the human species.

From biologic tests for the presence of progestin through pregnancy one might hope to show the duration of the physiologic activity of the corpus. Unfortunately, the hormone seems to be in such low concentration in the circulation that it has thus far not been recovered in blood or urine. Such a possible test would be further complicated by the demonstrated presence of progestin in placentae during the latter months of pregnancy.[8, 9] The assay for this hormone in human ovaries removed at different intervals after conception has not been done. There remains as a possible test of the life of the luteal body, a study of the duration of the characteristic response to this stimulus of the endometrial glands in the decidua vera.

The typical features of endometrial response to progestin are seen in the latter half of a normal menstrual cycle (see Fig. 1). In the preceding menstrual flow, the upper two-thirds of the mucous membrane lining the uterine cavity is shown, diagrammatically, to have

*Brief protocols are included at end of paper.

been cast off. By the second week after this bleeding started, the simple, tubular glands begin to show prolific mitotic activity in their columnar epithelial cells, and as a result they become greatly elongated, coiled, and twisted when seen in longitudinal section. The nuclei of these gland cells are tightly packed, long, narrow, and deeply stained through the first, or preovulatory half of a normal cycle. At about the fifteenth day, or soon after, ovulation occurs, and it is then that the elaboration of progestin brings about significant changes in the glands and epithelial cells; mitotic growth ceases and secretion begins. The glands become "saw-toothed," and are lined with swollen cells containing round, basal, clear-staining nuclei. Before menstruation the epithelium is cuboidal and secretory discharge distends the gland lumen. This modification into a secretory tissue is so clear-cut that there is generally little difficulty in demonstrating by these

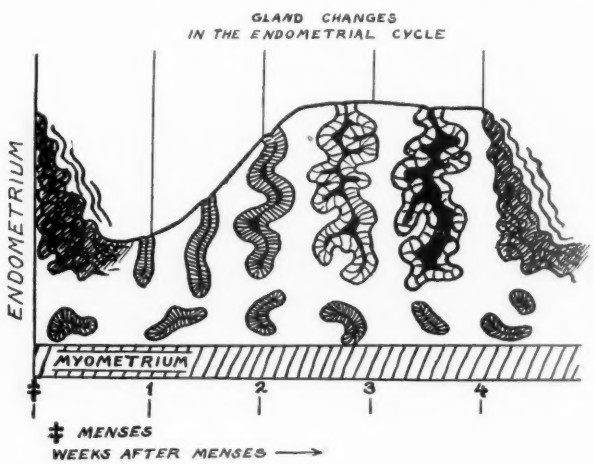

Fig. 1.

changes the presence of an actively functioning corpus luteum. It should be noted that throughout the normal cycle the basal glands, that is, the glandular roots lying near the myometrium, take no part either in proliferative activity or secretory discharge; throughout the month they remain static, inert. If the egg is not fertilized and implanted, then coincident with corpus luteum atrophy, the endometrium again breaks down in the next menstrual flow.

If, however, a fertile egg is implanted, the corpus does not involute but continues to grow and expand. The endometrial glands of early pregnancy reflect this continuation of progestin output by even more marked secretion than that seen during the preceding two weeks.

To study the duration of this secretory activity, surgical specimens of 13 uteri were selected with the object of observing such activity at approximately three-week intervals through pregnancy. None of these

specimens had been removed for local pathology that could have influenced the histologic appearance of the glands in the decidua. Specimens from both decidua vera and the decidua basalis were in most

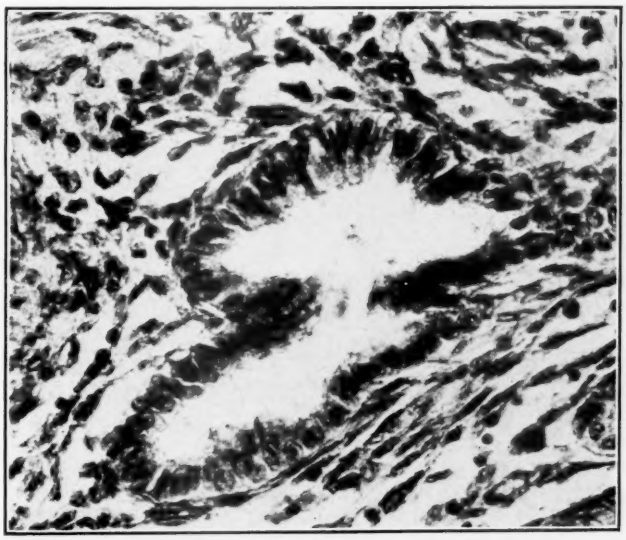

Fig. 2.—Six weeks' pregnancy; a decidual gland from basal layer showing neither proliferative nor secretory activity. Except where stated, these photographs are all from decidua vera. (Case S-36-753.)

Fig. 3.—Ten weeks' pregnancy; a decidual gland from spongy layer beneath implantation site. The cells are cuboidal, the nuclei round; this gland is in active function. (Case S-35-658.)

cases available. Photographs were made from some of these sections to demonstrate the progressive changes occurring in the glands during pregnancy.

Fig. 2, from a six weeks pregnant uterus, shows a gland from the basal layer, embedded in muscle tissue. The nuclei are long, narrow, deep-staining, in high columnar epithelial cells. Although glands in the upper layers of the decidua show

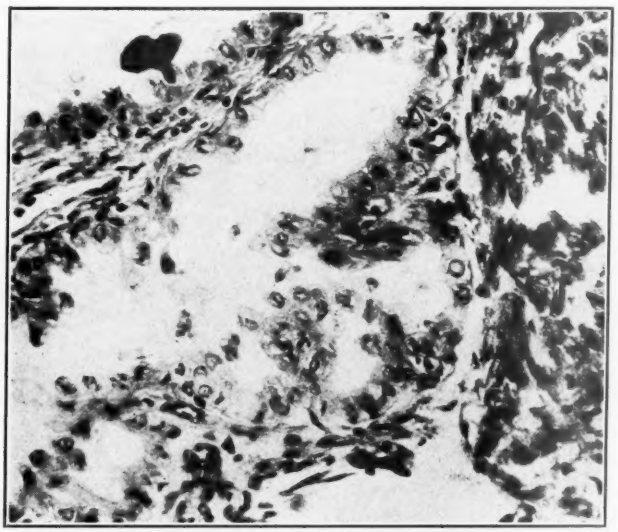

Fig. 4.—Eighteen weeks' pregnancy; a decidual gland from the basal layer showing evidence of active secretion. (Case S-36-498.)

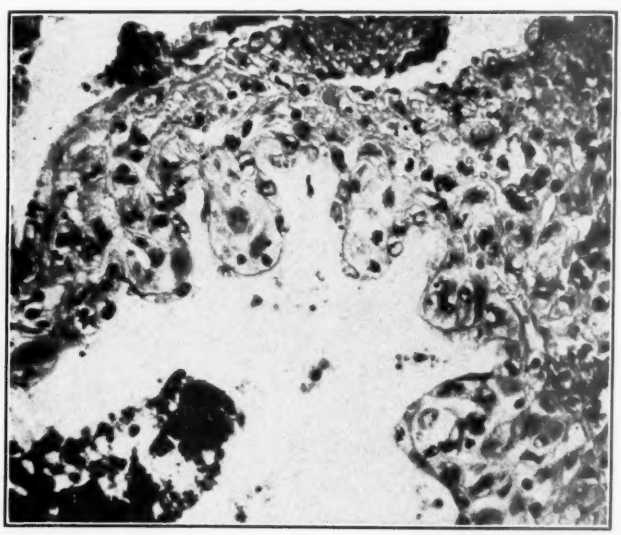

Fig. 5.—Twenty-three weeks' pregnancy; a decidual gland from spongy layer. The cells lining this gland are losing their epithelial characteristics. The lumen contains masses of cellular debris. (Case S-35-909.)

active secretion at this stage, there is here seen no evidence of any activity in the basalis glands.

A gland from the middle or spongy layer of a ten weeks decidua is seen in Fig. 3. The epithelial cells are cuboidal and contain round clear nuclei. The luminal

margin is indistinct and frayed. This section was from the implantation site, and the gland lumina are markedly swollen with secretion, possibly due to obstruction of the gland mouths by the growing trophoblast above. It may be this distention

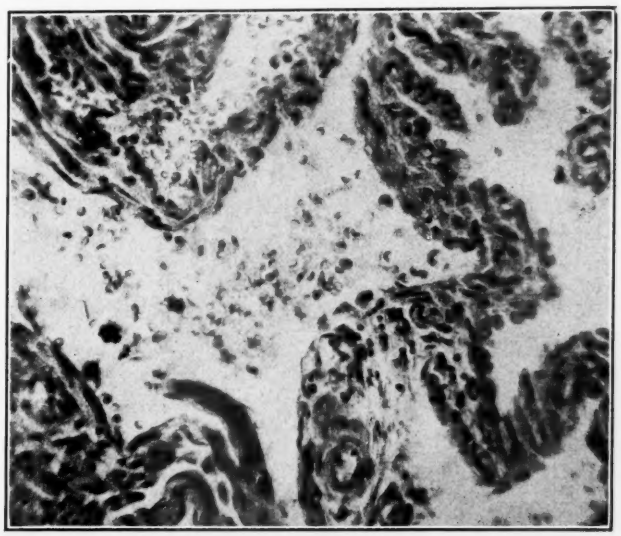

Fig. 6.—Thirty-two weeks' pregnancy; a decidual gland from spongy layer which has degenerated into a large irregular sinusoidal space containing blood cells and epithelial debris. (Case S-34-135.)

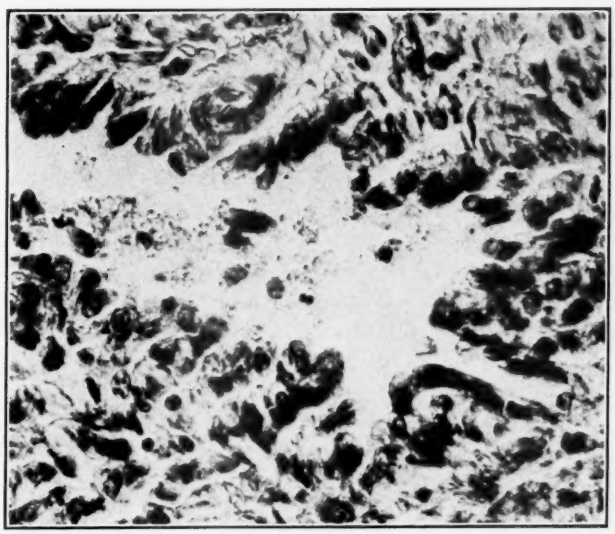

Fig. 7.—Thirty-two weeks' pregnancy; a decidual gland from basal layer showing degenerative changes. (Case S-34-135.)

that causes the lining epithelium to appear so flattened, but the cytology is definitely that of active secretion.

In Fig. 4, a gland from the basal layer, resting on muscle bundles, is again shown, from an eighteen weeks' pregnancy. At this stage these glands are secreting actively;

the clear, swollen cells with round nuclei are seen bulging into the lumen. It is of interest that the modification of the inactive basal glands shown in Fig. 2 into the functioning structures seen in Fig. 4 takes place without any demonstrable intervening phase of mitotic proliferation.

A gland from the spongy layer at twenty-three weeks is reproduced in Fig. 5. Here the gland lining is gradually losing its epithelial characteristics. These cells are thinning out, in places they are entirely missing, leaving the decidual stroma denuded. The large sinusoidal spaces that were once gland lumina are filled with débris, partly from infiltrating blood elements and partly from the degenerating epithelial margins.

At thirty-two weeks, this process of degeneration has progressed still further. In the upper decidual layers, the irregular spaces have almost the appearance of thin-walled lymphatic sinuses lined in places with endothelial-like cells (Fig. 6). It is only by tracing the glands from early pregnancy that one can confidently recognize

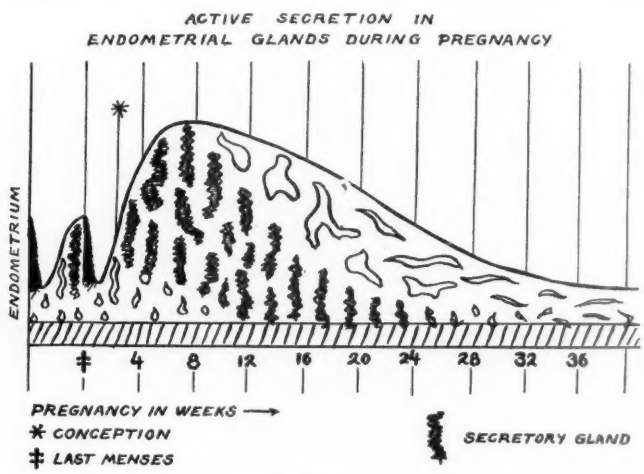

Fig. 8.

them as the origins of the spaces seen at eight months. In the basal layer (Fig. 7), at the same time, there is found no evidence of active function, and the cells lining the gland are apparently being cast off into the lumen.

The duration and extent of active secretion in the decidua vera as demonstrated in Figs. 2 to 7 is summarized in Fig. 8. At eight weeks there is found the greatest extent of activity in the upper layers of the decidua, though the basal glands have not undergone any changes. Beginning nearest the surface and gradually extending downward, there is a loss of glandular secretion shortly after the second month, and a coincident degeneration of the glands into large sinusoidal spaces. At the same time, there takes place a progressive functional involvement of the basalis layer. At the fifth month, only the gland structures near the myometrium show any activity, and by the seventh month all evidence of secretion is lost. It will be noted that the glands of the upper superficial layer, those nearest the surface and therefore, perhaps, most important in any function concerning a newly-implanted embryo, lose their activity about two months from the previous menses. It is also seen that the basal glands generally exhibit no significant activity except from about the twelfth to the twenty-fourth week of pregnancy.

DISCUSSION

The progressive nature of the glandular involvement demonstrated in this study is difficult to explain on the basis of variations in hormone stimulus alone. The character of the response in the decidual glands suggests that duration of secretion does not accurately reflect the length of life of the corpus luteum of pregnancy. The degeneration of these glands, appearing in those that react first and passing down to those influenced last, implies that their secretory function is limited perhaps by some factor intrinsic to the glands themselves rather than by a decrease in the stimulating mechanism. Thus, Hisaw[10] has described as an exhaustion phenomenon the involution of secretory glands in a castrate *Macacus rhesus* after twenty-four days of constant progestin administration. It is possible that the duration of secretion in the decidua vera is terminated by a similar "exhaustion" of the glands. Since progestin has been recovered from placentae at term where it is presumably available as a source of stimulus, the "exhaustion" hypothesis would explain the lack of any apparent secretion in the decidua at that time.

The secretory changes here studied are histologically similar to those resulting from response to progestin alone in an estrin-primed endometrium.[10] There is scant evidence that these changes can ever be maintained for weeks by progestin and estrin alone, from a "persistent luteoma," except in gestation. Since it is normally only in pregnancy that the pregnancy urine hormone (anterior pituitary-like hormone) is available to the organism, it is possible that this stimulus plays a part in the secretory response of the glands. It may be significant that recent quantitative assays for the pregnancy urine hormone[11] have shown a peak at the eighth week, with a gradual decrease to a considerably lower plateau thereafter. Although the addition of pregnancy urine hormone perhaps makes possible a longer glandular response than that which could be obtained without it, yet the decrease of pregnancy urine hormone after the eighth week does not necessarily explain the progressive quality of the glandular response described in this study.

SUMMARY

When pregnancy is complicated by an ovarian tumor, operative removal of the tumor may involve the corpus luteum. Evidence from the literature suggests that excision of the corpus luteum results in from 10 per cent to 33 per cent of miscarriages if done within the first two months. This evidence, however, is neither statistically accurate nor reliable. If a satisfactory test for the presence of the luteal hormone could be devised, it might be possible to determine the length of functional life of the corpus luteum. This would lead to a better under-

standing of the risks of removing the corpus luteum in early gestation. The characteristic response of decidual glands to progestin is the only available test, at present, for this hormone. The duration of this response was studied in specimens of uteri removed at approximately three-week intervals through pregnancy.

CONCLUSIONS

1. The nature of the secretory response seen in the decidual glands suggests that the duration of this activity cannot lead to positive conclusions concerning the length of functional life of the corpus luteum of pregnancy.

2. The maximum involvement of decidual glands in active secretion is found at about the eighth week in the most superficial zones of the decidua vera. This would appear to lend a certain amount of support to conclusions from evidence in the literature, that the corpus luteum cannot be excised within eight weeks from the last menses, without seriously jeopardizing the successful course of gestation.

PROTOCOLS

M. G. H. (Case 14390), married, aged 29 years, para iii, housewife, last menses Apr. 28, 1936. She was first seen June 21, 1936, complaining of steady low abdominal pain two weeks. She showed large retroverted uterus, and cyst in the right ovary. Operation June 22, 1936. A two months' pregnant uterus was left untouched. Large cyst right ovary necessitating removal of whole organ. Corpus luteum in cyst wall. Left ovary small, scarred, no corpora lutea. *Pathologic Report:* Lutein cyst. Following operation very slight amount of staining with mild cramps and clots June 25, 1936. This continued with passage of decidua and clots until July 1, 1936, when miscarriage apparently was completed, and from then on convalescence was uneventful.

P. H. (Case 31038), married, aged 29 years, housewife, one child, one miscarriage. Last menses Oct. 14, 1936. Seen Dec. 9, 1936, complaining of vague abdominal discomfort. Had had slight staining off and on for three weeks. Uterus definitely enlarged, cyst in right vault size of orange. Operation Dec. 10, 1936; two to three months pregnant uterus left untouched. Large cystic right ovary. Fluid aspirated and cyst wall resected. Left ovary inactive with neither follicles nor corpora lutea. *Pathologic Report:* Lutein cyst. In spite of 4 rabbit units of proluton on December 11 and December 12, patient bled freely with cramps on December 15; abortion then considered inevitable and curettage done Dec. 15, 1936, with uneventful convalescence.

B. M. (Case 16893), single, aged 21 years, student, examined Jan. 9, 1935, found to have uterus size of two and a half to three months' pregnancy. Right adnexa normal; left, definite mass 2 inches to 3 inches in diameter. History of introduction of blunt instrument two weeks before followed by slight bleeding for a few days. Exact date of last menses not known. Jan. 11, 1935, operation, normal pregnancy of at least two and a half months, uterus left untouched. Left ovary showed bilocular cyst size of a lemon; right ovary showed many follicles and old scars, no corpora lutea. Left ovariectomy performed. *Pathologic Report:* Follicle and lutein cysts. Course: normal postoperative recovery, but three weeks after leaving hospital and five weeks postoperatively, patient reported that she miscarried.

This study was made possible by the generous help and sympathetic cooperation of Drs. Arthur Hertig and Hugh Nuckols who placed material from the Pathology Laboratory of the Boston Lying-in Hospital at the author's disposal.

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270 Commonwealth Avenue

A COMPARATIVE STUDY OF POSTERIOR PITUITARY EXTRACT ADMINISTERED AT THE ONSET OF AND AFTER THE COMPLETION OF THE THIRD STAGE OF LABOR

F. Frederick Fortin, A.B., M.D., Chicago, Ill.

(From the Lewis Memorial Maternity Hospital)

THE active principle of the posterior lobe of the hypophysis cerebri, commonly called pituitrin, was introduced into the practice of obstetrics in 1909 by Blair-Bell. This innovation failed to attract much attention at first, but was generally adopted in 1911 following the studies and recommendation of Hofbauer. In the voluminous literature which followed here and abroad, we find occasional references to the advantages of using this oxytocic at the onset of the third stage of labor. This so-called prophylactic administration was cautiously introduced in anticipated postpartum hemorrhages, e.g., in hydramnios, following the delivery of twins or excessive babies, etc. As early as 1913, we read that Teufel and Rübsamen, independently and in the same year, administered this new oxytoxic as the baby's head was being delivered. The latter reported a reduction to one-third or one-fourth of the average blood loss.

Fellenberg, in 1914, brought the subject of prophylactic injection of the infundibular extract to the attention of the Gynecological Congress in Berne, and seven years later having used it routinely in this manner reported favorable results and advocated its prophylactic administration. In the same year (1921), Ryder administered the drug to 100 patients following the completion of the second stage of labor, and compared the results with an equal number of patients who did not receive an oxytocic. The conclusion reached was that this early administration "appeared to be safe and valuable in minimizing the blood loss." The following year Broadhead and Langrock corroborated the results in a similar series. Several other studies of the same nature appeared in the literature during the ensuing years. A dissenting voice was, however, heard during this wave of enthusiasm. Reist and Guggenheim, in 1923, after comparing three series each of 100 cases and using a different

preparation of the hypophysis prophylactically, in two series, and no oxytocic in the third, concluded that the routine prophylactic injection offered no real advantage in the majority of cases. The more recent studies of Scott (1925) and Jess (1926) concerned pituitary and nonpituitary series and were distinctly in favor of prophylactic administration.

Today it is an accepted fact that posterior pituitary extract reduces the postpartum blood loss, but the question is whether the early prophylactic administration is more advantageous than administration immediately following labor, and even whether it is not actually detrimental. A careful search of the literature has not revealed a single comparative study on the point in question. This is indeed surprising in view of the lack of agreement from authoritative sources. DeLee recommends it following the birth of the baby "where ideal maternity conditions are available." Davis and others believe that the third stage is shortened and hemorrhage decreased by early administration but state that "the use of posterior pituitary extract should be confined to Hospital practice, where complications of the third stage can be more safely managed than in the home." The late J. W. Williams always believed that "the excessive contraction as occasionally induced by solutions of pituitary is potentially productive of real pathologic changes." Calkins definitely states that it should be given "immediately after the delivery of the placenta, never before, because the constant (physiologic) contraction is necessary during the separation phase of the third stage." Urner believes the early administration of pituitrin "plays an important part in lessening the blood loss" and believes that the objection on the basis of hour-glass contraction is theoretical, "as this condition has not occurred with any greater frequency in a similar group of patients where no pituitrin was used after the first stage of labor."

I am herewith reporting the results of a comparative evaluation of a solution of the pituitary given at the onset and after the completion of the third stage of labor.

THE PRESENT STUDY

Over a period of thirteen months, we have administered 1 c.c. of a physiologically tested and standardized solution of the hypophysis containing 10 international units routinely by hypodermic injection, to 1,100 consecutive full-term and premature vaginal deliveries at the onset of the third stage of labor; we compared the results with a similar series in which the patients received the same medication immediately following the completion of labor. The oxytocic fraction (pitocin) was substituted in cases presenting a contraindication to the use of a solution of the whole posterior lobe, and solutions of ergot were used as indicated to control hemorrhage.

From Jan. 11, 1936, to Feb. 12, 1937, 2,340 women were delivered in the Lewis Memorial Maternity Hospital. Four maternal deaths occurred, hence the uncorrected mortality was 0.17 per cent. Expressed in terms of live births this was 0.177 per cent or 1.77 per thousand. For reasons stated further on, only one death is included in this series and that was the result of a postpartum hemorrhage. The uncorrected infantile mortality was 3 per cent.

Subtracting 27 patients delivered by cesarean section (an incidence of 1.1 per cent), and 28 whose babies weighed less than 1,500 gm. or measured less than 35 cm. in length, there were 2,285 full-term and premature vaginal deliveries. Eighty-five of these cases were not included in the study, because the blood loss was not measured or was inaccurately measured. In the nonmeasured or estimated group, there are included all patients delivered on the "septic floor" on which there was no equipment to measure blood, and the occasional precipitate deliveries. Inaccurate measurements resulted when unruly patients were delivered, or the attendant did not eliminate amniotic fluid, etc., or failed to collect all the blood. In this group the blood loss was sufficient in 7 cases to be classified as a postpartum hemorrhage, and the placenta was removed manually in 3 cases.

Thus 2,200 full-term and premature vaginal deliveries constituting 96 per cent of all deliveries in this class, over a period of thirteen months, offered material for analytical study. All patients were delivered by the resident staff and the obstetrician-in-chief. All but the more difficult operative cases were attended by young men (junior residents) who were starting to learn the principles of obstetrics. Two different groups cooperated in the study, and in order to make the comparison more valid, each group delivered approximately one-half the total number of patients in each series. It has been our custom to use as little analgesia as possible. In some cases morphine and a derivative of barbituric acid were given during the first stage, and all patients were delivered under ether, ethylene, or chloroform anesthesia.

The technique of management of the third stage as advocated by Calkins was adopted *in toto*. To quote: "Immediately after delivery of the baby, the hand is placed on the abdomen; the uterus is held very gently with the fingers behind and the thumb in front, and with no attempt to massage the organ unless it shows signs of relaxation and flaccidity. As soon as it changes from a discoid to a globular shape, and a trickle of blood appears from the vagina, the organ is vigorously massaged until it becomes firmly contracted and then, by squeezing and gentle downward pressure an attempt is made to express the placenta. Should the placenta not come out readily, no further attempt is made to express it, and no further massage is instituted until some sign of enlargement or flaccidity appears or there is an increase in bleeding from the vagina. Immediately after delivery of the placenta the uterus is again massaged to obtain firm contraction, and the hand is kept constantly in contact with the uterus for a period of one hour or until such time as the attendant assures himself that there will be no further tendency toward relaxation or flaccidity."

There is a wide difference in reports on postpartum blood loss from various representative clinics. A number of factors are undoubtedly

involved, a difference in technique of management of the third stage, the training and experience of the attending personnel, the type of patient, and what is perhaps most important of all, a difference in the method of measuring the blood loss. More uniform results would unquestionably be reported were a uniform method of measuring adopted. This, I believe, is well brought out in the present report.

The technique of measuring the postpartum blood loss in this study was developed in the Lewis Memorial Maternity Hospital and is based on the principle proposed by Pastore, whereby the blood is collected

Fig. 1.—The sterile chrome plated pan and trough directs the blood stream downward. The graduated glass collector is moved in or out of range of the flow by pressing the left knee against the projecting bar.

and the amount read at a moment's notice throughout the third stage of labor, including when necessary the blood lost just prior to delivery from a laceration or episiotomy, and excluding nonsanguineous flows such as amniotic fluid, urine, or antiseptic solutions. The apparatus has been greatly simplified without impairing its accuracy. Whereas Pastore deflected the flow of amniotic fluid by a movable trough attached to the collecting pan, we eliminate that by moving the graduated glass collector out of range of the flow. The deflection is effected at a moment's notice by knee action and a reading is possible at any

time. Fig. 1 shows one of three such blood measuring set-ups used in this study. In delivering each patient special attention was paid to (1) accurate measurements of postpartum blood loss, and (2) correct timing of the duration of the third stage of labor. Manual removal of the placenta was resorted to for strict indications only.

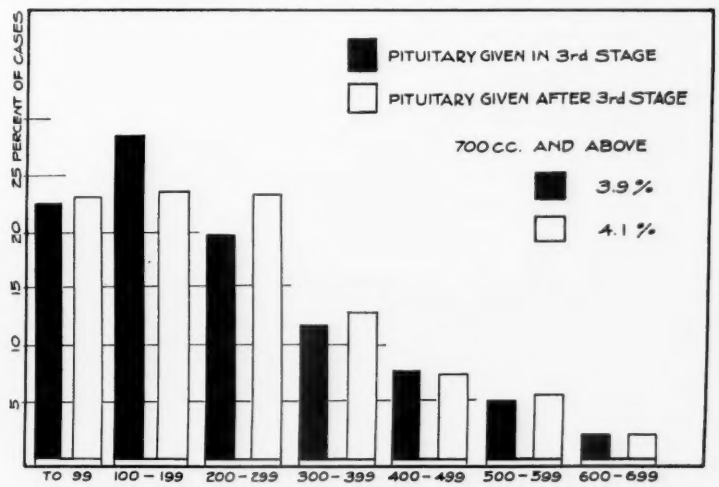

Fig. 2.—Blood loss in 100 c.c. groups.

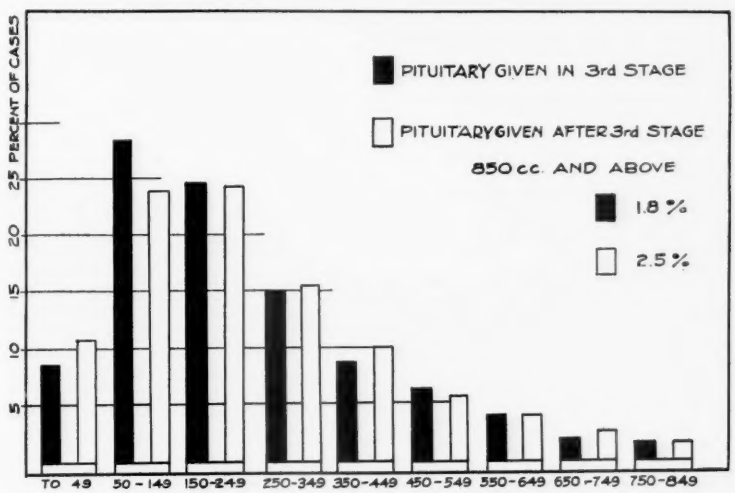

Fig. 3.—Blood loss in 100 c.c. groups.

COMPARATIVE RESULTS

The postpartum blood losses here reported are total losses for the period during which the patients remained on the delivery table, a minimum of one hour. The clots expressed during or at the end of that period are included. As a result, a considerable number of total losses were increased in amount.

If we arrange the total blood losses in groups of 100, starting at zero or at 50 c.c., and compare the group incidence, there is a striking similarity of distribution as seen in Figs. 2 and 3. The difference in the general average is negligible; it was 5 c.c. less in the series receiving the oxytocic prophylactically. The averages were 270 c.c. and 275 c.c.

The previous comparative studies involving prophylactic pituitary and nonpituitary series have shown a considerably greater advantage of the former. As before mentioned Rübsamen reduced the average loss from 300 c.c. to between 75 and 100 c.c., a reduction of 66 to 75 per cent of the average blood loss. Ryder using Williams' technique of measuring the blood loss, in a series of 200 cases demonstrated a reduction of 2⅓ ounces (70 c.c.), the averages being 5.9 ounces (177 c.c.) and 8.2 ounces (247 c.c.), a reduction of 30 per cent on the average. This study was corroborated by that of Broadhead and Langrock. Reist and Guggenheim denied the advantages heretofore demonstrated, claiming that in general the blood loss was unaffected by the prophylactic injection of pituitary. However, they maintained that it did lessen the blood loss in cases of atonia uteri, especially when associated with deep anesthesia and in repeated postpartum hemorrhages, in which cases only did they believe it was indicated. Scott's figures showed a reduction of 20 per cent of the average loss, a saving of 44.8 c.c., the average being 198.7 and 243.5. Using pituitrin prophylactically and intravenously Jess reported a saving of nearly one-half the average blood loss in normal and operative cases: his figures were 398.2 reduced to 187.8 c.c. and 655 reduced to 342 c.c., respectively.

In comparing our results with those already reported, the importance of a uniform method of measuring the postpartum blood loss is evident. Pastore reported an average blood loss of 244.3 c.c. in a series of 574 cases, as compared with our 275 c.c. In 70 per cent of his patients the blood loss was less than 300 c.c. as compared with 69.8 per cent in our series. In a later study he reported an average loss in 1,870 deliveries of 271.3 c.c. The average loss reported in the literature ranges from 179 c.c. (Calkins) to 500 c.c. (DeLee, Ahfeld, Sellheim). Tarnier's average of 600 c.c. is perhaps the highest on record. In Williams' clinic the average in 1,000 spontaneous deliveries was 343 c.c., and Plass using the same technique in a series of private cases reduced it to 317. The reduction is attributed to management by the experienced obstetrician in contrast to the young apprentice.

Calkins who is strongly in favor of administering pituitary solution only after the placenta has been delivered, reported an average blood loss of 222 c.c. and later with an improved technique in the management of the third stage (which we have adopted) reduced it to 179 c.c. with

89 per cent of the total losses below 300 c.c. His technique of measuring, as described in an earlier paper, includes estimation as a part of the total loss and, of course, introduces the personal element. In Urner's series of more than 7,500 cases in which pituitrin was given at the onset of the third stage, 86.9 per cent lost less than 300 c.c., but nothing was said of the method used in measuring the blood.

In Table I, the average results of spontaneous and induced labors are shown but are difficult to interpret. The majority of these cases were merely stimulated with oleum ricini and quinine during the course of a desultory labor. Those induced with solutions of pituitary

TABLE I. AVERAGE BLOOD LOSS IN RELATION TO TYPE OF DELIVERY

TYPE	PITUITARY EXT. BEFORE		PITUITARY EXT. AFTER	
Spontaneous		269 c.c.		277 c.c.
Induced	9%	288 c.c.	7.0%	261 c.c.
Normal		249 c.c.		264 c.c.
Operative	10%	423 c.c.	9.1%	450 c.c.

extract or by surgical means are included, but are too few to permit any conclusions. In the table, we see that induced and stimulated labors bled more than spontaneous labors when pituitary extract was given prophylactically, and less when it was given at the end of labor. The results appear inconsistent. In comparing normal and operative deliveries there is a small but constant advantage in the prophylactic administration. In normal deliveries 15 c.c. were saved and in operative 27 c.c. Analgesia in the form of barbituric acid derivatives administered during the first stage has, in our experience, increased the blood loss. In 200 cases the average blood loss was 295 c.c. and the incidence of hemorrhage was 7.4 per cent. This is more than 1 per cent higher than the general incidence of hemorrhage to be reported.

As suggested by Williams a total blood loss of 600 c.c. or more is considered abnormal, and classified as a hemorrhage. As seen in Table II, the prophylactic administration of pituitary extract reduced the hemorrhage by only 0.27 per cent. The average loss was reduced only 5 c.c. This, of course, is not a fair evaluation of the efficacy of pituitary extract, inasmuch as it cannot be expected to affect a hemorrhage resulting from a laceration, ruptured varix, etc. We shall return to this point in an analysis of hemorrhages in relation to causative factors. Our incidence of postpartum hemorrhage compares

TABLE II. EFFECT OF PROPHYLACTIC PITUITARY EXTRACT ON HEMORRHAGES

	NO. OF HEMORRHAGES	PERCENTAGE	AVERAGE LOSS
Pituitary Ext. before	66	6.0	837.4 c.c.
Pituitary Ext. after	69	6.27	842.5 c.c.

favorably with that of Pastore (6.4 per cent and 7.11 per cent in a later report), and of Peckham and Kuder (6.14 per cent). It is one-half that of Williams (13 per cent), less than that of Plass, and about twice as great as that of Calkins (2.5 per cent) and Urner (3.4 per cent).

TABLE III. HEMORRHAGES GROUPED AS TO CAUSES

	ATONY		MISMANAGEMENT		VARIOUS		HOURGLASS CONTRACTIONS
	CASES	PER CENT	CASES	PER CENT	CASES	PER CENT	
Pituitary before	35	50.7	24	34.7	9	13.0	1
Pituitary after	33	50.0	23	34.8	9	13.8	1

The results of an analysis of causative factors in Table III, show that the prophylactic administration of pituitary does not influence postpartum hemorrhages from an etiologic standpoint. The group termed atony includes cases of hydramnios, twin births, excessive sized babies, atony due to deep anesthesia or prolonged labor, as well as the primarily inactive uterus. If the prophylactic administration of pituitary extract has any value in reducing postpartum blood loss, it should certainly be evident in this group. Comparing the average blood loss in each series we find that the earlier administration reduces the hemorrhage from 1,060 to 885 c.c., a saving of 175 c.c., or 16.5 per cent.

The mismanagement group, referred to in Table III, includes cases having a major portion of the bleeding with expulsion of the placenta and those in which the placenta was prolapsed into the hollow of the sacrum. Cervical lacerations, deep vaginal tears, ruptured varicosities, retained cotyledons, and myomata uteri are grouped under "various."

Impressed by reports of Moir, Dale, Davis, Adair and others, we used ergonovine to control hemorrhages, giving 0.25 mg. intravenously. We have not witnessed any untoward reactions attributable to this drug. The prompt and lasting uterine response with resulting control of the hemorrhage has indeed been most gratifying. It was used in approximately one-half of each series, and following its introduction uterine tamponade was found necessary in only 0.23 per cent of cases as compared with 1.1 per cent before its introduction. The incidence of packing was therefore reduced 79 per cent.

The drug, however, was administered, but to no avail, in the fatal postpartum hemorrhage occurring during this study. A summary of the sequence of events in this case will now be presented.

M. W., a 33-year-old para iv, gravida vi, had an uneventful obstetric history. The physical examination was entirely normal except for moderate sized varicosities of

both legs. The pelvis was normal, blood Wassermann negative and hemoglobin 80 per cent. The antenatal course was normal in every way. She was admitted in very mild labor one week after the expected date of confinement, and on admission a definite hydramnios was noted. Seven hours after admission she was given 3 gr. of quinine bisulphate for three doses at half-hour intervals. Twenty-four hours later, not yet definitely in labor, she was given an ounce of castor oil followed by the same amount of quinine for four doses every half hour. Moderately severe labor pains followed at irregular intervals. When the cervix was 4 or 5 cm. dilated and the vertex at -1, the membranes were ruptured artificially but only a moderate amount of fluid exuded. She was now given a small dose of one of the barbiturates and one hour later delivered spontaneously a normal male infant weighing 8 pounds 13 ounces. Light open drop ether was administered for four minutes.

Immediately after the birth of the baby an enormous amount of amniotic fluid followed. This was then followed by a steady but moderate flow of blood. The

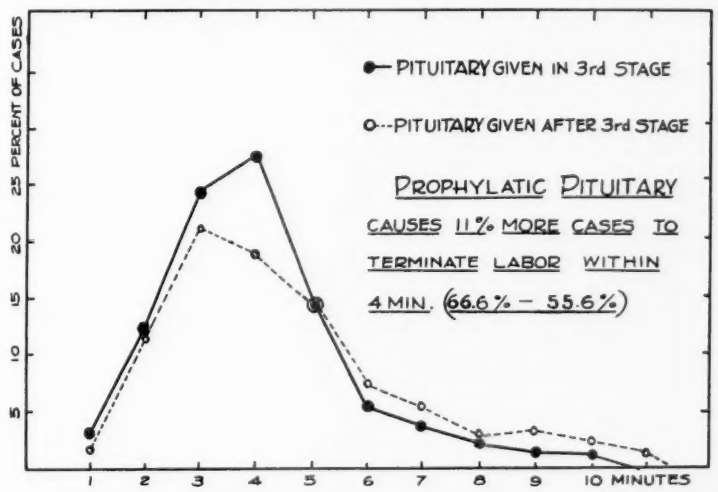

Fig. 4.—Length of the third stage.

placenta had separated and was expressed with the membranes one minute after the birth of the baby. One cubic centimeter of a solution of the posterior pituitary was given intramuscularly at this time. Bleeding continued and two minutes later 1 c.c. of a solution of ergot was given hypodermically. Three minutes later the blood loss totaled 800 c.c. and 1/320 of a grain of ergonovine was given intravenously. A 5 per cent solution of glucose was now started as the pulse was becoming rapid, although the general condition was not alarming. Because of continued bleeding, another ampoule of ergonovine was given in glucose solution, being administered intravenously. The birth canal and the uterine cavity were now quickly examined and a uterovaginal packing resorted to one-half hour after delivery when the blood loss totaled 1,400 c.c. Blood continued to ooze through the packing, and it was therefore removed and another packing inserted. The patient's condition was now critical. She died an hour and a half after delivery, as a blood transfusion was being given. An autopsy was not obtained. A careful postmortem examination of the generative tract revealed no lacerations or varicosities, and the uterine cavity contained numerous small walnut-sized clots. The total measured blood loss was 2,100 c.c. which represents 2.75 per cent of the patient's weight.

Fig. 4 shows the distribution of cases according to the time of separation and expression of the placenta, which using the Calkins technique should be practically simultaneous.

TABLE IV. BLOOD LOSS IN RELATION TO TIME OF PLACENTAL SEPARATION

	UP TO 2 MINUTES			3 TO 5 MINUTES			6 TO 10 MIN.			ABOVE 10 MIN.		
	NO.	%	AV.	NO.	%	AV.	NO.	%	AV.	NO.	%	AV.
Pituitary Ext. before	170	15.4	258.9	729	66.2	264.0	171	15.5	252.7	30	2.7	358.9
Pituitary Ext. after	163	14.8	272.0	615	55.9	258.6	260	23.6	294.0	62	5.6	387.3

There is a remarkable parallelism between the two curves, except at the points three and four minutes where a deviation is evident. It is clear that prophylactic pituitary causes 11 per cent more of the placentae to separate within four minutes, and this advantage (if it is an advantage) is practically confined to the three- and four-minute periods. It is, therefore, clinically evident that in the immediate postpartum period the infundibular extract acts in three to four minutes. It is generally believed by the proponents of prophylactic pituitary administration that the third stage is shortened and the blood loss thereby decreased.

A careful consideration of Table IV shows that the average blood loss is considerably increased, about 100 c.c. on the average when the placenta is retained over ten minutes. Of course in these cases, the bleeding episiotomy wound increases the total to some extent. The prophylactic administration reduced the incidence of such cases 2.9 per cent, and reduced the total blood loss by 29 c.c. or 7.5 per cent of the average loss. We may also assume that 8.1 per cent of the cases had a shorter third stage than six to ten minutes due to the early administration of pituitary extract, and the average blood loss was reduced 14 per cent. Below five minutes the prophylactic administration series includes 11 per cent more cases than the group in which pituitary was given after expulsion of the placenta. In this same group the difference in blood loss is not large enough to be significant, bearing in mind that the fatal hemorrhage undoubtedly accounts for the higher figure in the group termed "up to two minutes."

It would seem therefore that the optimum time for the separation and expression of the placenta is before five minutes, and while the earlier administration of pituitary extract does not lessen the bleeding in this group, it places 11 per cent more cases in the group. When the duration is longer than five minutes, prophylactic administration is effective in reducing the blood loss.

A comparison of the complications of the third stage of labor as shown in Table V might be interpreted as slightly in favor of the

series in which pituitary extract was administered following the expulsion of the placenta, but the difference is too small to be convincing.

In an effort to explain why the prophylactic injection of solutions of posterior pituitary does not frequently cause trouble, Calkins stated that "it requires from seven to ten minutes to produce a severely hard

TABLE V. COMPLICATIONS OF THE THIRD STAGE

	MANUAL REMOVAL OF THE PLACENTA			REMOVAL OF RETAINED COTYLEDONS	DILATATION AND CURETTAGE
	CASE	TIME	INDICATION		
Pituitary extract before	1	14 min.	Hemorrhage and hourglass contraction	5	1
	2	40 min.	Hemorrhage	Removed immediately	
	3	14 min.	Hemorrhage		
Pituitary extract after	1	2 hr. 2 min.	Retention	3	2
	2	1 hr. 35 min.	Hemorrhage Hourglass contraction	Removed immediately	

contraction of the uterus, and in a majority of instances the placenta will have been delivered before that time." The explanation does not appear adequate, because as shown in Fig. 4 it is clinically evident that pituitary extract acts in three to four minutes. Furthermore, kymographic tracings show that the first phase is a tetanic-like contraction which lasts several minutes, followed by waves of contraction and relaxation which are higher than the normal waves and decrease gradually in intensity.

Is it not probable that the hypersensitive uterus can be thrown into a state of disordered contraction by pituitary extract and thereby cause placental incarceration?

SUMMARY

The optimum time for the administration of pituitary extract in controlling postpartum bleeding is an unsettled question. A comparative study of the prophylactic administration *in* the third stage and administration after completion of the third stage is presented. The study involved 1,100 cases in each series and the results obtained are as follows:

1. The general average blood loss and the group percentage distribution are too nearly alike to concede an advantage to either method.

2. Investigation of induced and stimulated labors yielded inconsistent results.

3. There is a 5.5 per cent reduction of the blood loss in normal cases and a 6 per cent reduction of the average loss in operative cases when pituitary extract is administered prophylactically. The maximum saving is less than an ounce.

4. Prophylactic administration reduced the incidence of postpartum hemorrhage by 2.7 cases per thousand. It had no effect on the cause of hemorrhage, but did reduce the blood loss in hemorrhages due to atony by as much as 16.5 per cent. And inasmuch as the average postpartum hemorrhage with an atonic uterus amounted to 1,060 c.c., the saving was considerable.

5. The earlier administration of pituitary extract shortened the third stage of labor causing 11 per cent more patients to terminate this stage within four minutes. This helped to increase the number of cases in the group having the lowest blood loss.

6. If the placenta is delivered within five minutes, prophylactic injection does not lessen appreciably the blood loss. However where the third stage lasts between six and ten minutes, the blood loss is reduced 14 per cent, and where the placental stage requires more than ten minutes, the blood loss is reduced 7.5 per cent. But the average blood loss in these two groups is 250 and 380 c.c., respectively, and inasmuch as the percentage saved is inversely related to the amount of blood loss, the maximum saving does not amount to an ounce and a half.

7. The complications of the third stage are about equally distributed in both series.

CONCLUSION

The effective control of post-partum blood loss is the result of careful management of the third stage of labor based on a thorough knowledge of the physiology and pathology involved. The prophylactic administration of solutions of the pituitary body is not productive of more trouble, and appreciably reduces the blood loss in hemorrhages due to uterine atony only.

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ELDERLY PRIMIPARAE*

A Study of 240 Cases

Cloyce R. Tew, M.D., Raleigh, N. C., and
K. Kuder, M.D., New York, N. Y.
(From the Department of Obstetrics and Gynecology, Cornell University Medical College and New York Hospital)

WE BELIEVE that an unprejudiced reporting of the results encountered in any obstetric problem will result eventually in an accumulated experience which will correct or substantiate impressions, too often erroneous, and if not settle that problem, will erect certain landmarks of significance that may be useful in its proper management. This paper is an endeavor to conform to this premise by attempting to evaluate the rôle of age as it affects the course of pregnancy and labor in that group of patients who present themselves for obstetric guidance with their first pregnancies at 35 years or older, to add our results to the few, but none the less significant, contributions that have preceded ours, and to which we have largely conformed in outline, in order that such observations and conclusions as we shall be able to offer can be more readily correlated and their value be more clearly deduced.

A review of the literature, which is characterized by the scant number of the American contributions in contrast to the large number from France, Germany, and the Scandinavian countries, indicates that there has not been accorded, in this country, this interesting and important subject the attention which it deserves. From the literature available the significant articles are not numerous; the majority of them dealing with such abstract angles of the subject as the economic, social, and other prevailing conditions, which have resulted in the large and ever increasing number of elderly primiparae; and spend little time with the actual personal study and analysis of such women and the reporting of observations that might assist in formulating an intelligent basis for prognosis and treatment in their care.

What constitutes an elderly primipara? The controversy on this point in the literature, to assign this term to any age group has proved as indefinite and unsatisfactory as have most attempts at medical classification. From limits as widely separated as 28 to 40 years denoting the upper limit of youth, we find that the majority of writers have established this boundary at 30 or 35 years. In accepting and following the dividing line as 35 years, we feel we have accepted the

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proper one and are following the custom of most writers, particularly the American obstetricians. Hence, we define an elderly primipara as that patient who has undertaken pregnancy in the latter years of the childbearing period, and in consequence one who has her baby between the ages of 35 and 45 years. A negligible number escaping this classification, due to the extreme of age, would, of the fact of their occurrence, constitute a problem all their own.

It can certainly be deduced by an inspection of the figures presented by different authors, notwithstanding a few of their more hopeful interpretations, that as far as toxemias, operative deliveries, morbidity and mortality rates are concerned most of the figures show beyond doubt the tremendously higher incidence of these complications in the elderly primiparae. We cannot pass without calling attention to the fact that many of the maternal deaths were postoperative after cesarean section. Von Khreninger-Guggenberger and Leutenmeyer caution against the use of cesarean section in elderly primiparae as being especially hazardous even with excellent indications, believing that these elderly primiparae do not stand the operation well, and in their thirteen operations they had four deaths.

Our cases are from the service of the Lying-In Hospital in New York where during the four-and-one-half-year period from Sept. 1, 1932, to March 31, 1937, there occurred on the indoor service 11,919 deliveries with the birth of 12,059 infants. Of this number there were 240 patients that fell into the elderly primiparae group, an incidence of 2.01 per cent. This figure agrees with that of most writers. It was found in most groups that the incidence is higher in private patients than in clinic groups. We have not made this distinction in the reporting of our material.

In our series, elderly primiparae showed an incidence of contracted pelvis of 15.5 per cent, differing not appreciably from that of the total clinic population, which is 14.4 per cent. However, on analysis of these contractions of the pelvis, they are in agreement with the statement frequently made that the major type of pelvic contraction in the elderly primiparae is of the funnel variety and is much higher than the incidence of this type in the younger primiparae.

In Table I we have attempted to list, so far as possible, the most significant complications of pregnancy and give their incidence in relation to the control series. The incidence is approximately the same in contracted pelves and the occurrence of cardiac disease. In our series the incidence is greater in the case of the toxemias (almost 3 times), placenta previa (2 times), and myomata uteri, which is almost double the clinic figure. The high incidence of these complications may be extremely serious and may influence the ultimate prognosis in a given pregnancy. The incidence of a previous abdominal operation in

our elderly primiparae was 22.0 per cent. Some of these operations would conceivably not be carried out on younger individuals; but in the last analysis operations such as cervical amputations, myomectomies, ectopic pregnancies, and salpingectomies from all causes, as well as some types of uterine suspension, should be considered a distinct factor in trying to offer a prognosis to such a patient and due to her age might influence the handling of such a patient at term. The literature is full of cases so complicated from previous abdominal operations, and the outcome in such cases in a significant percentage has been unsatisfactory to both mother and child.

TABLE I. COMPLICATIONS OF PREGNANCY

	INCIDENCE	
	ELDERLY PRIMIPARAE	TOTAL CLINIC POPULATION
Contracted pelvis	15.5%	14.4%
Cardiac disease	3.7%	3.9%
Toxemia	22.5%	8.1%
Syphilis	0.4%	1.0%
Tuberculosis	1.2%	0.4%
Myoma uteri	8.3%	4.9%
Placenta previa	0.8%	0.5%
Pyelitis	2.5%	1.3%
Epilepsy	0.4%	0.1%

Table II shows the complications of labor, which we have listed in the manner of several other authors. We have compared these to our control series of the general clinic population. The greater incidence of occipitoposterior positions, arrested transverse positions, and postpartum hemorrhage is remarkable. Of great significance is the large

TABLE II. COMPLICATIONS OF LABOR

	INCIDENCE	
	ELDERLY PRIMIPARAE	TOTAL CLINIC POPULATION
Persistent occiput posterior	11.2%	8.4%
Floating head at term	53.3%	20.9%
Postpartum hemorrhage	8.7%	6.7%
Arrest in midforceps	7.1%	4.5%
Placenta previa	0.8%	0.5%
Prolonged labor	17.1%	11.2%
Prolonged second stage	34.6%	19.0%

percentage of elderly primiparae who come to term with the head of the child unengaged (53.3 per cent, in contrast to that in the control series 20.9 per cent). The operative incidence in this group of elderly primiparae (being only about half of the total elderly group) is 68.8 per cent and 41.9 per cent in the control group. To state it differently we may say that at term with the head floating the incidence of spontaneous delivery in the elderly primiparae is only 31.2 per cent compared to 58.1 per cent in the control group. The most significant

reference showing the seriousness of this complication is that given by Schultze who states that this one finding must be considered a definite danger signal. Supporting this, and it is typical of many, she cites the cases of unengaged heads in her series in which there were 36.8 per cent cesarean sections; and in addition there were 44.4 per cent dystocias noted in the remaining, only 11.1 per cent had easy labors; the fetal mortality was 27.7 per cent and the maternal mortality was 1.7 per cent in this group.

This one reference we considered of sufficient seriousness to justify any precautions that may be militated for the elderly primiparae and we believe it tends to substantiate our statement earlier in our remarks that the hazards associated with childbearing in the elderly primipara are of very certain existence. Certainly no one would have us believe that the figures given are in any measure comparable to a control series of young primiparae or a clinic control series of all ages. Does it not then follow that in any group where the operative incidence is so high, the results so uniformly poor, it is well to consider this group of patients a weighty obstetric problem in which one is more likely to meet more serious difficulty and the assumed risks are greater?

The incidence of different presentations in our elderly primiparae is approximately the same as in our control clinic series.

The shortest labor among the 240 elderly primiparae was 2 hours and the longest 102 hours. Compared to the control group, labor in elderly primiparae was definitely prolonged, i.e., 17.1 per cent compared to 11.2 per cent. Likewise in the elderly primiparae the second stage was prolonged over the clinic group, i.e., an incidence of 34.6 per cent compared to 18.0 per cent. Whatever may be the cause of this prolongation of labor in all its stages, be it rigidity of the perineum, rigidity of the cervix, poor uterine contractions, or congenital hypoplasia and a faulty isthmus, albeit the fact remains that this finding of prolonged labor is greater in the elderly primiparae, and its reflection in the course of labor and the type of delivery is all too apparent and many times the results appalling.

A significant and interesting set of figures appears in Table III, illustrating the type of delivery in our series contrasted with those of the control series. All operative procedures are higher in the elderly primiparae, i.e., 56.7 per cent instead of 25.1 per cent. Now many people claim that a high incidence of operative cases in elderly primiparae is not as serious or significant as in the younger patient, due to the fact that most of the operations consist simply of terminating the second stage prophylactically by low, or at best by midforceps. In order to refute this we turn to one of the best series published on elderly primiparae (Schultze) and find that in this group there were 35 patients assisted in the first stage; 28 manual dilatations; 4 cases

of Dührssen's incision; and 3 cases of dilatation aided by the insertion of a bag. In most series the indications for interference are not given and, true, many may be as intimated above, but this we know: that in our series none of the operative deliveries were done on the indication

TABLE III. TYPE OF DELIVERY

	INCIDENCE	
	ELDERLY PRIMIPARAE	TOTAL CLINIC POPULATION
Spontaneous	43.3%	74.9%
Forceps (all types)	36.6%	14.9%
Cesarean section (all types)	12.9%	3.6%
Breech extraction	4.5%	4.4%
Version and extraction	1.6%	0.7%
Craniotomy	0.4%	0.1%

of prophylaxis or on the indication of elderly primipara per se, except for 2 cesarean sections. We adhered to the clinic standard, in all cases, for the operative indications applying to all patients, hence it may be said that the same complications necessitating the employment of operative methods in the termination of labor in the elderly primiparae are twice as high as that of the clinic control group.

TABLE IV. INDICATIONS FOR CESAREAN SECTIONS

TYPE	NO. OF CASES
Placenta previa	2
Premature separation	2
Disproportion (trial labor)	2
Disproportion (contracted pelvis)	6
Pelvis and spine deformity	1
Contracted pelvis and breech	1
Acute yellow atrophy	2
Disproportion (infection), Latzko	1
Myoma uteri obstructing inlet	4
Myoma uteri (transverse presentation)	1
Cervical dystocia	2
Preeclampsia	1
Contracted pelvis and cervical stenosis	1
Contracted pelvis and recent myomectomy	1
Chronic nephritis (sterilization)	1
Chronic nephritis	1
Myoma uteri and extreme funnel pelvis	1
Premature rupture of membranes with disproportion	1
Elderly primigravida	2

Several authors do not hesitate to fall back upon "elderly primiparae," as an indication for cesarean section. In our series all sections were done for pure obstetric indications, except the two cases previously referred to. It is one of the purposes of this study to determine whether or not broadening the indications for cesarean section in this group of patients would give better results than the indications we now rigidly adhere to. We believe that all the cesarean section operations in this group of elderly primiparae were performed on

proper obstetric indications, and therefore an incidence of 12.9 per cent shows that there are certainly about three and one-half times more complications arising in elderly primiparae that demand cesarean section than in the ordinary clinic group. The figure of 12.9 per cent represents an irreducible minimum which is in marked contrast to the clinic figure of 3.6 per cent; and if to this we add other sections on an "elderly primiparae" indication we might find ourselves reporting a figure so high that of itself it would be incompatible with any known sound obstetric system.

The incidence of episiotomies was 67.9 per cent in contrast to 62.8 per cent in the control series. This figure is not as high as that given by most authors who hail this procedure as a boon to the elderly primiparae and report 80 to 90 per cent performance of this procedure. To us our figures show that as far as the perineum is concerned in vaginal deliveries, the contention of some that perineal rigidity is great, cannot be taken without reservation, and that there must be other and more serious factors, which we have tried to point out, to explain the high operative incidence with its subsequent reflection in the mortality and morbidity rates.

The weights of the infants of elderly primiparae do not vary essentially from the clinic group. In marked contradistinction to the opinion usually held that the children of elderly primiparae are generally of excessive size, it may be said that the largest series of such reported shows the weights of the babies born to women of this age group to be smaller by 240 gm.

TABLE V. CAUSES OF INFANTILE MORTALITY

Prolapsed cord	2
Toxemia of mother	6
Syphilis	2
Antepartum hemorrhage	2
Malformation	2
Intracranial hemorrhage	4
Contraction ring	1
Intrapartum infection	1
Cord about neck	1
Cause unknown	5
Gross infantile mortality	10.7%
Gross infantile mortality, total clinic population	4.1%

We present our figures on infantile mortality in Table V. By "infantile mortality" is meant all premature and full-term infants, deadborn, stillborn, or dying within fourteen days following birth. We report a gross infantile mortality of 10.7 per cent in contrast to 4.1 per cent in the control series. We find some of the reports to have corrected figures. We have given our figures as gross in order that they may be evaluated by those interested. The infantile mortality, as re-

ported by the various authors, is in general agreement with the figures we report. It is to be noted that there is no agreement in the literature as to what constitutes fetal mortality, certain authors reporting only full-term stillbirths, others deleting all cases where the fetal heart was not heard at the beginning of labor. It is for this reason that we advocate the term "infantile mortality," as defined above, because it reveals complete information as to the fate of the child.

Our maternal mortality, uncorrected, in the elderly primiparae, was 1.25 per cent in contrast to 0.2 per cent in the clinic control. The causes of death in the three cases were cardiac disease, questionable acute yellow atrophy, and peritonitis following cesarean section, respectively.

By "puerperal infection" is meant a rise in temperature to 100.4° F., or 38° C. which occurs once during each of two 24-hour periods following delivery or remains elevated longer than 24 hours, excluding the first 24 hours after delivery, unless the rise in temperature is definitely proved to be due to other causes, such as mastitis, pyelitis, or intercurrent infection. Morbidity includes all cases of puerperal infection and all those febrile from other causes. In this study we have observed a marked difference between the incidence of morbidity in the elderly primiparae and that in the clinic control group, the former being 21.6 per cent and the latter 11.4 per cent; while the incidence of puerperal infection is likewise elevated in the elderly primiparae to 12.5 per cent as compared to 8.6 per cent for the whole clinic.

There are other aspects of this problem about which it is difficult to obtain data but which are none the less important. One of the most important is that (discussed by Leopold Meyer) concerning the difference between the primiparae who married late in life and promptly conceived and those who married early and did not conceive until late. It is our impression, from the patients where this information was available, that in the latter group the complications mentioned in the total series of elderly primiparae are considerably more in evidence, i.e., the labor is somewhat longer; the operative incidence relatively higher; the toxemias occurred more frequently; and not the least important is that their labor was more likely to be of the weak unsatisfactory kind which we have come to speak of as desultory type. We believe their behavior in pregnancy and parturition is influenced by certain constitutional factors as well as some stigmata of genital hypoplasia, and these patients would probably not be ideal obstetric subject matter at any age. This group, however, forms only a small portion of our total series (2 to 5 per cent), and it is contended that here is only one, although perhaps the most important, of several factors involved.

SUMMARY

We have called attention to the widespread impression entertained by both the laity and the profession that elderly primiparae are more prone to the serious complications of labor and pregnancy and that in entering into this group the patient assumes a greater risk than her younger sister. We have attempted to show, by the use of our clinic material, that these apprehensions are in some measure well founded by actual obstetric experience and not "tradition" as it has been so often called. We have given available figures from the literature on many of the salient features of "elderly primiparae" which, in the main, have substantiated our conclusions that there is a marked increase in the incidence of toxemias, particularly the more serious types; that the operative incidence is at least double that of the ordinary clinic population; that the infantile mortality is markedly elevated; that the maternal mortality is four times greater than the clinic population; that labor is definitely prolonged and that morbidity and puerperal infection rates are significantly increased.

It is to be hoped that with the advances being made in obstetrics, particularly in the fields of endocrinology and x-ray pelvimetry, we may soon have at our disposal means of prognosticating more accurately in a given case the dangers that are to be avoided and so be more properly equipped to guide these patients through their pregnancies at a time when the value of a child is perhaps relatively greater. Premature induction of labor and the broadened indications for the employment of cesarean section operations do not, in the light of the figures studied, seem to clarify to any significant degree the manifold phases of the problem of elderly primiparity. By publishing the results of actual cases studied, uncorrected, and by making available to others whatever measures have served to improve the results in any given complication; together with what we may be able to gather from the advances now in progress, we may hope to bring about considerable improvement in both morbidity and mortality.

Until these methods are at our disposal, it is unwise to proceed on the assumption that elderly primiparae differ very little from the younger primiparae.

From our evidence presented, we are forced to conclude that an elderly primipara presents a distinct problem to the obstetrician and, consequently, that the teachings of some of the earlier writers to the effect that these women are more prone to the serious complications of gestation and parturition are well founded.

CONCLUSIONS

1. The incidence of elderly primiparae (35 years of age and over) is 2.01 per cent in a series of 11,919 obstetric patients.

2. There is an increased incidence, among elderly primiparae, of toxemia of pregnancy, placenta previa, and myoma uteri.

3. Although there is no marked difference in the total incidence of all types of contracted pelves in this group of women, funnel pelves are definitely more predominant than among younger primiparae.

4. Among the complications of labor in elderly primiparae, we note an increased incidence of occipitoposterior positions, arrested transverse positions, and postpartum hemorrhage. We also observe that the head of the child is unengaged at term in 53.3 per cent of elderly primiparae, as compared with a figure of only 20.9 per cent in a control series of patients.

5. The operative delivery incidence is greatly increased in the elderly primiparae, being double that of the clinic population.

6. Maternal mortality is definitely higher in the elderly primiparae group, than in the total clinic group of patients.

7. Infantile mortality, which includes premature, full-term and neonatal deaths, is markedly elevated in elderly primiparae, being almost three times that of the clinic population.

8. The elderly primipara does not seem to be able to undergo operative procedures at delivery with as good results to herself, as does the younger woman as shown by the complications of the puerperium.

9. "Elderly primipara," per se, does not constitute an indication for cesarean section, unless there is an accompanying complication, which still further adds to the risk to the offspring.

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Watson, E. M.: Carcinoma of Female Urethra, J. Urol. **35**: 654, 1936.

Carcinoma of the female urethra now is being encountered and recognized much more frequently than formerly. It may appear in the third but usually occurs in the fifth decade of life. A positive Wassermann reaction may be present and so mar one's best efforts in arriving at an early diagnosis. A single biopsy specimen may be misleading. In spite of a report "no malignant condition found" the patient should be carefully watched and, when healing is unduly delayed, further sections obtained. One fourth of the patients in the author's series of seventeen had had "growths" removed from the urethra previously, a predisposing factor to malignant changes. Early recognition and properly instituted treatment give an appreciable measure of palliation. A four-year cure and probably longer may be expected in more than 50 per cent of the cases.

J. P. Greenhill.

PNEUMOCOCCUS INFECTION OF THE GENITAL TRACT IN WOMEN

Especially During Pregnancy and the Puerperium

Hugh H. Nuckols, M.D., and Arthur T. Hertig, M.D., Boston, Mass.
(From the Departments of Obstetrics and Pathology, Harvard Medical School and the Boston Lying-in Hospital)

Aufrecht[1] demonstrated, in 1884, that the puerperal uterus of animals is a locus minoris resistentiae when pneumococci are injected into the blood stream. This finding was confirmed by Ortmann.[2] Weichselbaum,[3] in 1888, found pneumococci in the endometrium and small uterine vessels in a case of fatal abortion during the course of a lobar pneumonia. Despite these and similar findings, American obstetricians and gynecologists have, if the literature is a criterion, shown but little interest in the subject of pneumococcal genital infections. The study of pneumococcal peritonitis and the allied genital infections has been carried on predominantly by pediatricians and surgeons.

These uncommon infections deserve more study than they have generally received not only because of their relation to occasional postpartum gynecologic manifestations in these patients, but also because they are so frequently expressions of an endogenous type of puerperal infection. They thus serve to remind us that endogenous infections do occur, and that organisms other than the streptococcus cause puerperal sepsis.

In this hospital three cases of pneumococcal puerperal infection have been identified during the six-year period from 1931 to 1936 inclusive. During this period there have been 20,364 deliveries in the hospital and outpatient department. All of these cases of infection of the genital tract have been secondary to pulmonary involvement. To be sure, other instances of pneumococcal pneumonia during the period of gestation and the puerperium have occurred during this period, some of which were fatal, but in only these three cases has the genital tract been shown to be involved in the disease process.

Case 1.—(M. M. UH 10084.) The patient, a twenty-four-year-old white tertigravida, secundipara, between thirty-seven and thirty-eight weeks pregnant, was admitted Feb. 9, 1933, with a history of ruptured membranes of forty-eight hours' duration. Except for known latent syphilis the past medical history was not significant. Physical examination was negative. The pelvic measurements were consistent with a generally contracted pelvis. Labor was allowed to progress until the sixtieth hour when the patient was delivered by a low transverse cervical

cesarean section, because of combined cervical and pelvic dystocia. The infant weighed 5 pounds, 7¾ ounces, and was in good condition. There was a moderate postoperative reaction, the temperature ranged from 99° to 100° F., the pulse was 120. On the fourth postoperative day the patient had a productive cough. The sputum was thick and greenish. Temperature 101° F., pulse 120, respirations 30. The clinical course was variable for two days, the cough became less productive, temperature 98.8° F., pulse 120. (At this time the infant was transferred to the Eye and Ear Infirmary with ophthalmia neonatorum.) On the ninth postoperative day x-ray study revealed a "typical lobar pneumonia" of the right upper lobe, but the temperature remained normal and the pulse was 100. On the fifteenth postoperative day the temperature, pulse, and respirations were rising and examination revealed an extension of the pneumonic process to the right lower lobe. On the twenty-first day the patient developed a septic arthritis of the right shoulder and elbow joints, which were swollen, hot, and very painful. The temperature, pulse, and respirations again rose sharply. From this time the patient's course was generally downhill, the temperature rose to 106° F., the pulse to 140. The patient became comatose and died on the twenty-ninth postoperative day.

In brief, the necropsy findings were: lobar pneumonia, involving the entire right lung; pneumococcemia; acute vegetative endocarditis—pneumococcal; pneumococcal meningitis; thromboses of the superior vena cava, right jugular, subclavian, axillary and brachial veins and the uterovesical venous plexus. Pneumococci, which were not typed, were recovered from the lungs, tricuspid vegetations (where they were associated on smear with some gram-negative diplococci), meninges, uterus, and various thrombi. Unfortunately no note was made of an examination of the inflamed joints. While a concomitant gonococcal bacteremia cannot be ruled out, the principal pathogen seems clearly to have been the pneumococcus.

Case 2.—(E. G. UH 11160.) The patient, a twenty-nine-year-old secundigravida, primipara, approximately thirty-eight weeks pregnant, was admitted Dec. 30, 1935, with a history of a cold of two weeks' duration culminating in malaise, sudden chill, fever, pain in the chest, and dyspnea. Her previous obstetric and medical histories were essentially negative. On admission the temperature was 101° F., the pulse 120, the respirations 28. Physical examination confirmed the diagnosis of lobar pneumonia involving the left lower lobe. The following morning sputum typing revealed Type I pneumococci and serum therapy was instituted. During the day 110,000 units of combined Types I and II pneumococcus antiserum (Felton) was administered intravenously. The blood culture taken on admission revealed a Type I pneumococcus. The patient seemed clinically improved but serum therapy was continued because of the positive blood culture. On the fourth hospital day the second blood culture, taken before the administration of the last serum, also proved positive for pneumococci. At this time the patient's antibody titer, as determined by Dr. Finland of the Boston City Hospital, was found to be high. On the fifth day following admission more serum was given as the blood culture was again positive. Six days after the onset of her illness the patient spontaneously went into labor and delivered a full-term normal male infant. Up to this time she had received slightly more than 400,000 units of the combined serum. Clinically she seemed improved but physical examination suggested encapsulated fluid at the left base and a thoracentesis was done. Typical greenish yellow creamy pus was obtained which on culture yielded a pure growth of Type I pneumococcus. Following this the patient's course was irregularly febrile and on the sixth postpartum day she was transferred to the Massachusetts General Hospital for drainage of the empyema. There her subsequent course was uneventful except that following drainage of the empyema on the left she developed a subcutaneous abscess, due to

the same type of pneumococcus, in the tissue over the right ninth rib in the mid-axillary line. She convalesced uneventfully and was discharged well.

The placenta of this patient was most interesting as it showed a localized area of premature separation, with an associated septic ischemic infarct. In Giemsa and Gram stained sections through this area many Gram-positive diplococci, some of which were encapsulated, could be seen invading the infarcted area. The same organisms were found also in the maternal blood and fibrin along the decidual plate.

CASE 3.—(E. J. UH 3516.) The patient, a twenty-seven-year-old quadrigravida, tertipara, approximately thirty-two weeks pregnant was admitted Jan. 28, 1936, complaining of chills, fever, and a productive cough. Her obstetric and medical histories were negative until two days prior to admission when she experienced headache and general malaise. Twelve hours prior to admission she had a sudden chill, pain in the left chest, fever, and cough. On admission the temperature was 104° F., the pulse 120, the respirations 40. Physical examination revealed some râles and suggestive bronchial breath sounds at the left base posteriorly. The following day there were definite signs of lobar pneumonia involving the left lower lobe. The sputum was typed and a Type II pneumococcus found. 200,000 units of combined Type I and II pneumococcus antiserum (Felton) were given intravenously in divided doses and the patient seemed definitely improved. That evening she spontaneously delivered a premature 3 pound, 4 ounce female infant by the breech mechanism. The baby was in poor condition from birth and subsequently died in the premature nursery. The next day the patient's temperature rose slightly and she appeared definitely more sick. Prognosis at this time was guarded. The admission blood culture contained Type II pneumococci and further serum was administered. On the fourth postpartum day the temperature was 103.8° F., the pulse 125, the respirations 38. The patient's general condition was poor. She had now received a total of 400,000 units of the combined serum. Blood cultures following the last serum treatment were repeatedly negative. Consolidation had spread, however, to involve the upper left lobe. The patient had foul lochia. Culture of the endocervix and lochia at this time yielded an almost pure culture of Type II pneumococci. An obstructing cervical plug was removed when the culture was taken. This improved uterine drainage. Simultaneously the patient began to improve steadily. Four days later the temperature was ranging between 98° and 99.5° F., the pulse was steady at 90. At this time there was noted some fluid in the left pleural space but repeated x-ray studies showed it to be resorbing and soon it had completely disappeared. The cervical cultures now proved negative, and on the twenty-eighth postpartum day the patient was discharged well. The placenta was carefully examined in this case but no evidence of any pneumococcal inflammatory process could be found.

The first of these cases demonstrated genital involvement in a widespread pneumococcal process. The organisms were not typed. The second case was shown bacteriologically to have identical type pneumococci in the sputum, blood stream, and pleural effusion. Associated with this was the finding of morphologically typical pneumococci in the placental infarct and in the maternal blood and fibrin along the decidual plate of the placenta. This lesion may illustrate the mechanism whereby the uterine wall is infected during a bacteremia. The third of these cases was shown bacteriologically to have similar type

pneumococci in the sputum, blood stream, and lochia. This was a case of true pneumococcal endometritis. It is of some interest, also, to note that all three cases occurred during the winter season.

REVIEW OF LITERATURE

Reports of pneumococcal puerperal infections have appeared almost entirely in the foreign literature, with but occasional reports originating in this country. The following cases have been found in a study of this literature and, with the exception of those noted as quotations from Bondy[11, 12] and two abstracts,[26, 34] have been verified by reference to the original articles. The classification of these cases, based on these reports, is of necessity a loose one. There is some overlapping in the groups and one group is included only because of the valuable comparison it offers. "Puerperal infections" include some instances in which no definite genital involvement was proved but was assumed as no other source of infection was found. Similarly "peritonitis in pregnancy—undelivered" includes three cases without definite genital involvement, but is closely allied to the puerperal infections and consequently of interest to obstetricians and gynecologists. The division "infection associated with abortion" is included as a separate entity in order to compare those infections occurring early in pregnancy with those occurring in the last trimester. To further complete the review and furnish a worthwhile contrast to the more generalized infections a group of "localized abscesses" is included. No attempt has been made to review pneumococcal peritonitis in general, though many of these cases, e.g., those of Lambert,[4] Gibson[5] and Peck[6] are of interest in any discussion of the source of these genital infections.

Whence comes this infection of the generative tract? This has been a subject of contention almost since the first cases were reported. Many of these patients were presented by their authors as having had a primary infection ascending through the generative tract, in contrast to a secondary or hematogenous infection. In many of the so-called primary cases the validity of such an assumption is subject to doubt due to incomplete examination, and in none was the source definitely proved. The remaining cases have been presented as complications of a pneumococcal process elsewhere in the body, or in the absence of any history as examples of an interesting uncommon lesion.

The earlier authors believed that either primary (ascending) or secondary (hematogenous) infections could occur but emphasized that a primary source could be assumed only after every possible older focus was eliminated by thorough clinical, pathologic, and bacteriologic studies. The lungs and heart were held by Bondy[10] and Hornung[39] to be the two major primary foci that were to be eliminated. This attitude practically demanded a complete autopsy study before assuming a primary source. Lord and Nye[53] in studying the pneumococcus found it could not long survive at the pH of the normal vagina, which as shown by various authors and

CASES FROM LITERATURE

AUTHOR	CLINICAL COURSE IN BRIEF	PNEUMOCOCCUS IN—	OUTCOME*	REMARKS
		"Puerperal Infections"		
Apert[7]	Peritonitis in puerperium associated with empyema	Pleural pus Peritoneal pus	R	
Armitage[8]	Abdominal pain, normal delivery, lungs clear	Peritoneal pus	D	
Baetjer[9]	6 wk. pp. developed salpingitis and pelveoperitonitis, *later* lobar pneumonia with bacteremia	Peritoneal pus Blood	R	Type II
Idem	5 wk. pp. developed sudden peritonitis, lungs clear until terminal pneumonia	Peritoneal pus	D	
Idem	Multip. 8 mo. pregnant developed peritonitis	Peritoneal pus	NS	
Bondy[10]	Normal delivery, manual extract. of secundines, peritonitis, lungs clear	Peritoneal pus Lochia	D	
Brawerman[11]	Spont. delivery, sepsis with endometritis, endocarditis and meningitis	Endometrium Endocardium Meninges	D	
Bumm[12]	Lobar pneumonia in puerperium, peritonitis	Lochia Uterine vessels	D	
Burckhardt[13]	Lobar pneumonia, spont. delivery	Placental site Uterine lymphatics	D	Pneumoc. in shoulder joint in life
Idem	Spont. delivery, sepsis with meningitis on second pp. day	Endometrium Meninges	D	
Canon[14]	Normal delivery, sepsis, death on twenty-first pp. day	Thyroid abscess Ovarian abscess Blood (PM)	D	
Czemetschka[15]	Lobar pneumonia, normal delivery	Meninges Endocardium Uterine lymphatics	D	Infant died of pneumonia
Darre, Laederich and Mamou[16]	Normal puerperium until onset of peritonitis	Peritoneal pus	R	
de la Marniere[17]	Gastric distress antepartum, normal delivery, peritonitis later assoc. with suppuration of dermoid cyst	Peritoneal pus	R	
Foulerton and Bonney[18]	Forceps delivery, sepsis	Lochia	D	
Idem	Pneumonia, premat. delivery at 7½ mo., death	Blood, lungs, spleen, uterus	D	

*R, recovered; D, died; NS, not stated.

CASES FROM LITERATURE—CONT'D

AUTHOR	CLINICAL COURSE IN BRIEF	PNEUMOCOCCUS IN—	OUTCOME*	REMARKS
Idem[19]	Term delivery, sepsis	Lochia Placental site	D	
Idem	Term delivery, retained membranes	Uterus Vagina	R	Associated with *B. coli*
Laffont, Castanier and Lavalle[20]	Term delivery, eclampsioid symptoms due to meningitis	Infant	D	Mother not posted
Laffont and Ezes[21]	"Cold," normal delivery, sepsis, pelvic phlebitis	Pelvic veins	D	A rare case
Levy[22]	Pneumonia, premat. delivery at ninth mo.	Pleural pus (mother) Blood and lungs of infant	D	Infant died at forty-ninth hour
Lop[23]	Normal delivery, douche, sepsis, lungs clear	Lochia Peritoneal pus	R	
McCord[24]	Normal delivery, peritonitis on third pp. day, laparotomy, lungs clear	Peritoneal pus Blood	D	
Idem	Spont. delivery, peritonitis, death on fourth pp. day	Peritoneal pus Blood	D	
Monckeberg[25]	Normal delivery, sepsis, lungs clear	Blood, lochia Peritoneal pus	D	Pneumoc. in throat of midwife
Pruska[26]	Op. delivery, endometritis, pneumonia *later*	Lochia (second day) Lungs and uterus	D	
Idem	Op. delivery, meningitis, lungs clear	Meninges Uterus	D	
Schuhl[27]	Manual removal of placenta, endometritis, pleurisy	Lochia	NS	
Seymour[28]	Low forceps, peritonitis, lungs clear	Peritoneal pus	R	
Smith and Spriggs[29]	Bacteremia on fourth pp. day, lungs clear	Blood	D	Primary source assumed Uterus not examined
Stravoskiadis[30]	Breech extr. with craniotomy, endometritis	Lungs, uterus	D	
Idem	Developed pneumonia on first pp. day	Lungs, uterus	D	
Wetzel[31]	Pneumonia, spont. delivery, peritonitis, operation, death	Lungs, peritoneum Infant	D	No definite uterine involvement, infant infected
Zangemeister[32]	Puerperal endometritis	Lochia	NS	

CASES FROM LITERATURE—CONT'D

AUTHOR	CLINICAL COURSE IN BRIEF	PNEUMOCOCCUS IN—	OUTCOME*	REMARKS
		"Peritonitis in Pregnancy" (Undelivered)		
Elkin[33]	7 mo. pregnant, lobar pneumonia, peritonitis	Sputum, blood Peritoneal pus	D	
Federici[34]	6 mo. pregnant, peritonitis. Heart and lungs clear	Blood and urine	D	
Harteman and Lacourt[35]	Bilat. lobar pneumonia, peritonitis	Lungs Peritoneal pus	D	Fetus also had pneumonia
		"Infections Associated With Abortion"		
Bondy[10]	Abortion, sepsis associated with old endocarditis	Blood Uterus	D	
Cohn[36]	3 mo. postabortum, metritis, meningitis. At post: retained placenta. Lungs clear	Meninges, spinal fluid, endocardium, endometrium	D	
Federici[34]	Abortion, bacteremia, associated with pleuritis	Blood Uterus	D	
Foa and Bordoni-Uffreduzzi[37]	Lobar pneumonia, abortion at fourth month	Uterine veins Fetus	D	
Idem	Lobar pneumonia, abortion at sixth month	Uterine veins Fetus	D	
Foulerton and Bonney[19]	Incomplete septic abortion at 3 mo. Lungs clear	Lochia	R	
Fricke[38]	Abortion, bacteremia and peritonism	Blood	R	Serum therapy
Hornung[39]	Induced abortion, sepsis, meningitis, lungs clear	Blood, spinal fluid, lochia	D	
Idem	Induced abortion, sepsis with cardiac signs	Blood (life)	D	Uterus not examined
Idem	3 mo. pregnant, incomplete abortion, meningitis	Spinal fluid, blood and lochia	D	
Jensen[40]	3 mo. pregnant, abortion. No history of pulmonary involvement	Peritoneal pus	D	Mixed with *B. proteus*
Stravoskiadis[30]	6 mo. pregnant, lobar pneumonia, endometritis	Lungs Endometrium	D	
Idem	4 days postabortum devel. meningitis. Pneumonia	Lungs Endometrium	D	
Vlach[41]	Abortion, D. & C., sepsis, terminal pneumonia	Blood (life) Meninges	D	Mixed with staph.
Weichselbaum[3]	Pleuritis, abortion	Pleural pus Endometrium Uterine vessels	D	

CASES FROM LITERATURE—CONT'D

AUTHOR	CLINICAL COURSE IN BRIEF	PNEUMOCOCCUS IN—	OUTCOME*	REMARKS
Wolfsohn[42]	3 days postabortum peritonitis, lungs clear	Peritoneal pus Lochia and uterus	D	
Idem	20 days postabortum, peritonitis	Peritoneal pus	R	
	"Localized Abscesses" (Tubal, Ovarian and Pelvic)			
Bondy[10]	No history	Pyosalpinx	NS	
Idem	No history	Pyosalpinx	NS	
Canon[14]	Assoc. with uterine Ca.	Pyosalpinx Peritoneal pus	D	
Cole[43]	Lobar pneumonia, pelvic abscess	Sputum Pus from pelvis	R	
Fricke[38]	No history	Pyosalpinges-bilateral	NS	
Frommel[44]	Last puerperium febrile after op. delivery	Pyosalpinx	D	Patient had apical tuberculosis
Gibson[5]	Pelvic symptoms for 2 years. Incision and drainage	Pus	R	
Hartmann and Morax[45]	No history	Pyosalpinx	NS	
Idem	No history	Pyosalpinx	NS	
King[46]	No pulmonary involvement	Tuboovarian abscess	R	
Idem	"Flu" prior to admission	Pelvic abscess	NS	Type IV
Idem	"Cold" associated with present illness	Pelvic abscess	NS	Type IV
Pearce[47]	No history	Pyosalpinx Peritoneal pus	D	
Ploeger[48]	No history	Pyosalpinges-bilateral	D	
Idem	No history	Pyosalpinges-bilateral	D	
Idem	Uterine Ca. with associated pelveoperitonitis	Pyosalpinx Pelvic pus	D	
von Rosthorn[49]	Febrile puerperium, 6 years of abdominal symptoms. No pulmonary history	Pyosalpinx	R	
Tompkins[50]	No history of pulmonary involvement	Pelvic abscess	R	Type I
Idem	No history of pulmonary involvement	Tuboovarian abscess	R	Type IV
Idem	Past history of pneumonia	Tuboovarian abscess	R	Type III
Witte[51]	Normal delivery 5 years previously, lungs clear	Tuboovarian abscess	R	
Wolfsohn[42]	Pulmonary tuberculosis	Pelvic abscess	R	
Zweifel[52]	No history of old focus	Tubal masses	R	

most recently by Oberst and Plass,[54] varies between 4.0 and 5.0. Shutt[55] working on the problem of wound infection by pneumococci substantiated this and concluded therefore that pneumococci could not enter the uterus as an ascending infection. But it has been shown by various workers[54, 56, 57] that the vaginal pH varies widely, apparently as a result of a disturbance of the normal symbiosis of the vagina and microorganisms of the group *B. acidophilus*. Injury to the vaginal wall, massive contamination and dilution and constitutional weakness are several of the factors which may disturb this symbiosis. Chronically ill and debilitated patients tend to have an alkaline reaction. Abraham[58] has shown this also to be true for children, thus confirming McCartney's[59] observation of the correlation of alkaline vaginal reaction in children with pneumococcal peritonitis. Similarly it has been shown[54, 56, 57] that the complexity of the vaginal flora increases directly as the pH rises. On this basis we must admit that a primary genital infection is possible, more especially in the parturient than the pregnant patient, if vaginal acidity is the defensive mechanism it has been assumed to be. King[46] basing his arguments primarily on the work of McCartney believes the primary source is the common one.

That this is so is most questionable in view of the many foci of pneumococci in the apparently normal person, notably the middle ear and nasopharynx. That a bacteremia or meningitis can follow spread of the organism from these foci without the intervention of a pulmonary infection is now accepted as fact. This is the explanation given in the cases of so-called "primary" peritonitis in the male. In all probability some of the cases reviewed in which a meningitis occurred were cases of this kind. An interesting case illustrating this process is the following:

CASE 4.—(L. McK. UH 12877.) The patient, a twenty-eight-year-old white sextipara delivered spontaneously, at home, a normal 8 pound, 4 ounce infant. When seen by a physician approximately one-half hour later, the placenta was still adherent and could not be expressed by gentle Credé method. The patient had bled nearly 1,000 c.c. and was in beginning shock. She was given emergency shock treatment and transferred to the hospital, where, on admission Jan. 22, 1934, the blood pressure was 60/0, the pulse thready and rapid, the skin cold and moist. As soon as possible she was transfused with compatible blood. The clinical improvement was rapid, therefore the patient was prepared and the placenta removed manually. Further improvement was aided by a second transfusion while the patient was still in the operating room. On the fourth postpartum day the patient had a sudden chill, the temperature rose to 103.4° F., there were a few coarse râles at the left base posteriorly, and the patient had a slight cough. This condition was but transient and the next day the temperature had returned to normal and cough disappeared. Her course was afebrile for five days and on the ninth postpartum day she was allowed to sit up. On that day she had a vaginal douche. The next day the patient got up but soon returned to bed complaining of general malaise and a headache. Shortly after this she had a sudden chill. The temperature rose to 104° F., the pulse to 140, accompanied by marked nausea and vomiting. Physical examination at this time was reported as negative. Two hours later she had a generalized convulsion which began in the upper extremities. Six hours later there was beginning rigidity of the neck and Kernig's sign became positive. Spinal puncture was done and 40 c.c. of antimeningococcic serum was given intravenously

when the spinal fluid was found to be turbid though under normal pressure. Study showed this fluid contained 2,500 W.B.C. per c.mm. and many Gram-positive diplococci, which on culture proved to be pneumococci. The patient's course was constantly downgrade, and she died twenty-eight hours after the onset of the initial chill. Clinically the sequence of events was believed to be: pelvic phlebitis, pulmonary embolus, and septic meningeal embolus from the lung.

At necropsy the lungs and heart were found negative throughout, as was the genital tract. There were found an acute tracheolaryngitis, a pneumococcemia and a pneumococcal meningitis. Postmortem cultures of the meninges and blood were positive for the pneumococcus, the antemortem blood culture remained sterile. In the absence of so complete an examination, this case might well have been assumed to be of primary genital source, especially with the history of manual removal of the placenta. Search for a pneumococcal focus in either the pelvis or lungs was, however, unavailing. The acute tracheolaryngitis seems the probable source of the organisms causing the meningitis.

Study of these cases of pneumococcus infection in the future may, with typing of the organism, be much more clearly defined as to source. For the present we must agree with Bondy and Hornung that either type of infection is possible but the assumption of a primary source is permissible only after exhaustive study—clinical, bacteriologic, and pathologic.

Twenty-three pneumococcal infections of all types occurred during the period under study. This is an incidence of 1 in 855 deliveries. Of these three, or 1 in 6,788 deliveries, had a pneumococcal genital infection. It seems probable that this incidence is low and that more careful bacteriologic studies will differentiate more true pneumococcal infections from that heterogenous group of infections attributed to *Streptococcus viridans* or "nonhemolytic" streptococcus.

From a statistical summary of the reviewed cases we can learn something of the prognosis:

	RECOVERED	NOT STATED	DIED
37 Puerperal infections	9-24.3%	3-8.1%	25- 67.6%
3 Peritonitis in pregnancy			3-100.0%
17 Infections associated with abortion	3-17.7%		14- 82.3%
57 Total diffuse infections	12-21.0%	3-5.3%	42- 73.7%
23 Localized abscesses	11-48.0%	6-26.0%	6- 26.0%

While these figures, obviously, are not to be taken as showing any more than a trend they do show the marked difference between diffuse and localized infections. Our own cases suggest that the prognosis in cases treatable by a specific serum appears definitely improved.

Prophylaxis is, of course, the major consideration in a discussion of the treatment of these conditions. General antenatal care seems the best prophylactic measure. The incidence of pneumococcal infection is said to be lower in pregnant women than in the general population. Whether it is the dislike of meeting strangers while large with child and the resultant avoidance of crowds, thus decreasing the probability

of exposure, whether it is the increased general resistance and good health due to adequate medical supervision, whether there is some possible specific immunity inherent in the pregnant state, or a combination of these factors, that is responsible for this lower incidence, is not known. Tompkins'[50] statement that saliva is a potentially dangerous lubricant for condoms implies that the ascending route must at all times be a negligible one as undoubtedly this is the most common of the lubricants, especially among the poorer classes. No particular prophylactic measures during labor and the puerperium are indicated other than the usual careful treatment of the patient.

The treatment of a generalized pneumococcal infection, including peritonitis, should be a conservative one with the addition where possible of specific antisera. The treatment of the localized lesion is surgical drainage.

SUMMARY AND CONCLUSIONS

Three cases of pneumococcal puerperal infection have been presented. The pertinent literature has been reviewed and the abstracted cases tabulated. All three of our own cases were endogenous in type. While many of the cases reviewed were thought to be of exogenous origin, none can be definitely proved so and an endogenous source appears more probable in most. That the exclusion of an endogenous source requires very complete clinical and laboratory studies is illustrated by a reported case of nonpuerperal pneumococcal infection.

The incidence of known pneumococcal puerperal infection in this hospital is one in 6,788 deliveries. It has been pointed out that this incidence is probably low due to the failure to identify organisms loosely classed as "nonhemolytic" or "green" streptococci. The prognosis in the localized infection has been shown to be much better than in the diffuse process. Treatment appears to be greatly aided if a specific antiserum is available.

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AN EXPERIMENTAL STUDY OF ACIDOSIS AND ALKALOSIS IN LABOR*

W. T. Pride, M.D., J. R. Reinberger, M.D., and D. T. Holland, M.D., Memphis, Tenn.

(From the Department of Obstetrics, University of Tennessee)

THE necessity of the normal alkali maintenance for health has been clinically appreciated for many years. Formerly, a patient free of organic disease was assumed to be a sound subject for any gynecologic or obstetric procedure. The physiologic approach to analysis of sudden unaccountable deaths has revealed that many were due to marked disturbances in the blood alkali acid ratio. Several years ago one of us encountered a severe alkalosis in a patient thought physically fit following a prolonged anesthetic for a simple gynoplastic procedure. The patient failed to respond to the available therapeutic measures, i.e., hypertonic salt solutions and blood transfusions. More recently a second patient received a prolonged gas anesthetic for an operation on a rather extensive pelvic inflammatory condition. Several hours after operation, she went into shock associated with complete anuria. The anuria was intermittently overcome by the introduction of glucose solution, but to our astonishment the carbon dioxide estimation revealed a fairly marked alkalosis of 78 instead of an acidosis as anticipated. In other words, both of these patients, in excellent condition, had received a prolonged gas anesthetic and presented the

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blood CO_2 evidence of alkalosis. Moreover, chloride contents had not been lost during postoperative vomiting which is recognized as a factor in this alkali acid imbalance.

Patients evidencing mild shock to extreme collapse at the time of delivery have been observed innumerable times. Quite often it has been encountered very shortly after the beginning of the anesthetic, but more often accompanying the necessary deep anesthesia for the termination of dystocias. Past judgment has always labeled such tragic complications as cardiac failure, pulmonary embolus, surgical shock and if death ensued, postanesthetic deaths. Recent observation and studies upon such patients long in labor have revealed occasionally the presence of acetone and diacetic acid in the urine, while the blood CO_2 estimation almost consistently showed the presence of severe acidosis.

An interview with a supervising nurse of an obstetric service even before this study was begun disclosed the possible cause for the presence of acetone and diacetic acid in the urine. She remarked "that the anesthetist requested fluids to be limited at least during the second stage of labor, so as to avoid the vomiting associated with anesthesia." Further inquiry revealed that many patients received very little food due to the discomforts of labor and analgesia. The forcing of fluids and the giving of food has eliminated this type of acidosis. Therefore, it was assumed to be a mild starvation and dehydration acidosis resulting from the limitation of fluids and food. The giving of glucose intravenously as a prophylactic in all cases in labor over thirty hours before an anesthetic or obstetric operation is started has also played an important part in bringing about such gratifying results.

Further blood studies of patients dying after long and difficult labors showed the presence of a marked acidosis which failed to respond to the usual combative measures, i.e., glucose and insulin. This inclined us to believe that either of the extreme alternations in alkali acid ratio may be reached before death and that this is a primary or important contributory factor, which if recognized or corrected may reduce the unfavorable results. It so happened during our routine blood CO_2 estimation of normal labor, that a patient was admitted after having been in labor for five days. She was in extreme shock with low blood pressure and a rapid pulse. The skin was cold and clammy. The blood CO_2 was 15 volumes per cent. The urine showed no acetone and diacetic acid. This has been a frequent finding in extreme labor acidosis. Glucose and insulin were administered with no response such as had been noted in previous cases. As a result of this experience, we decided to conduct a clinical experiment with the hope that this patient's condition could be more effectively combated. One of us suggested sodium bicarbonate solution intravenously, as this has been used successfully in controlling the severe acidosis of uremia. Accordingly, a 2 per cent solution of sterile sodium bicarbonate was given and the blood CO_2 estimations recorded. There was a distinct CO_2 elevation and the patient's general reaction was favorable, and it

appeared as though she would recover. This improvement was not sustained and death followed. It is now felt from recent experiments in dogs that this combination glucose and sodium bicarbonate solution may result in a chemical incompatability of a toxic nature, because death followed its administration in each of the 5 dogs to which it was given. In spite of this unfavorable reaction of the sodium bicarbonate and glucose combination, we still felt the need for a rapid neutralization agent that could be introduced into the circulation without harmful effects.

The literature contains many articles concerning the relationship of acidosis to normal pregnancy and labor. Mention is made of its ever present association in the toxemias. In an attempt to explain this commonly reported finding, a series of blood CO_2 studies in normal labor were carried out, dehydration and starvation acidosis being eliminated by proper fluids and food. The urine of these patients did not show the

TABLE I. CO_2 READINGS ON 157 PATIENTS—FIRST STAGE OF LABOR

PATIENTS	READINGS	PATIENTS	READINGS	PATIENTS	READINGS	PATIENTS	READINGS
1	51.0	41	40.0	81	40.0	121	44
2	39.0	42	35.30	82	35.0	122	41
3	54.0	43	32.0	83	47.0	123	45
4	43.0	44	46.0	84	30.0	124	38
5	51.30	45	25.0	85	38.6	125	43
6	24.30	46	48.0	86	44.0	126	45
7	45.0	47	49.75	87	43.2	127	44
8	40.0	48	49.0	88	41.75	128	43
9	54.60	49	54.75	89	35.0	129	33
10	46.0	50	37.0	90	39.6	130	33
11	48.0	51	55.30	91	21.6	131	48
12	57.0	52	56.0	92	24.0	132	39
13	48.0	53	42.60	93	41.6	133	44
14	45.0	54	42.60	94	39.0	134	45
15	55.60	55	38.0	95	42.0	135	44
16	50.30	56	51.0	96	43.0	136	52
17	42.0	57	35.0	97	38.6	137	51
18	45.30	58	44.0	98	41.75	138	28
19	38.0	59	43.0	99	43.2	139	44
20	54.0	60	32.0	100	25.0	140	45
21	52.60	61	40.0	101	50.0	141	44
22	38.60	62	48.0	102	43.0	142	52
23	41.75	63	45.0	103	39.3	143	51
24	46.30	64	45.0	104	46.3	144	28
25	39.30	65	44.0	105	50.0	145	48
26	40.0	66	42.0	106	54.75	146	46
27	24.0	67	46.0	107	48.3	147	44
28	26.0	68	53.0	108	40.0	148	51
29	41.30	69	48.0	109	41.3	149	49
30	54.0	70	36.0	110	50.3	150	49
31	42.0	71	44.0	111	46.0	151	37
32	58.6	72	44.0	112	52.0	152	31
33	47.6	73	40.0	113	46.0	153	45
34	44.0	74	43.0	114	47.0	154	43
35	51.0	75	31.0	115	45.0	155	44
36	44.0	76	46.0	116	41.0	156	40
37	35.30	77	42.0	117	48.0	157	44
38	50.60	78	26.0	118	38.0		
39	31.0	79	48.0	119	51.0		
40	37.0	80	31.0	120	46.0		

presence of acetone and diacetic acid. There was a constant lowering of the blood CO_2 as labor progressed, which reached the lowest point at the end of the second stage with recovery to normal immediately following delivery. This is in accord with most observations. The interesting fact was that the degree of acidosis was always in direct ratio to the hours and character of labor. This increasing acidosis was assumed to be the accumulation of lactic acid resulting from increased muscular activities. While we recognize the desirability of estimating the normal lactic acid content during labor, this was beyond the scope of our department which is essentially clinical with very limited biochemical facilities.

Table I presents the blood CO_2 estimations done in 157 patients during the first stage of labor. The lowest was 21.6 vol. per cent, the highest 56 vol. per cent. The average reading for the 157 patients was 42.98 vol. per cent. This indicates a moderate acidosis for the average, but the ones of interest are those with extremely lower readings who in some instances unless combated would pass over to a pathologic state. Therefore, it is advisable to keep in mind the possibility of such patients with a tendency towards the greater degrees of acidosis.

EXPERIMENT 1. ACIDOSIS PRODUCED BY ETHER ANESTHESIA

DOG	CONTROL	DURATION OF ANESTHESIA	2ND CO_2	DECREASE	INCREASE	CONDITION OF DOG
6	50 Vol. %	20 min.	42%	8 Vol.		Normal
7	57 Vol. %	20 Min.	48%	9 Vol.		Starved 3 days
8	46 Vol. %	35 Min.	35%	11 Vol.		Starved 3 days
9	52 Vol. %	30 Min.	55%		3 Vol.	Moderate starvation
10	None	20 Min.	38%			Normal
10	38 Vol. %	45 Min.	31%	7 Vol.		Good
11	45 Vol. %	20 Min.	42%	3 Vol.		Good

The anesthetic was not carried to the end point, but there is a decrease in the blood CO_2 in proportion to duration of the anesthetic. There is an average decrease of 7.3 vol. per cent for the ether anesthesia of twenty-five minutes. This verifies the previous statement that anesthesia produces and intensifies the acidosis.

Table II includes the blood CO_2 estimations of 65 patients done during the second stage of labor, the average 40.05, lowest 29 and highest, 53.30. These observations substantiate the previously made statement that the acidosis increases as labor progresses and is intensified by the character of labor. The longer and more difficult the labor the greater the acidosis.

Table III includes 50 patients immediately after delivery. The average was 48.9, lowest 29.2 and highest 86.6. This observation records the immediate response of the blood CO_2 to normal after the cessation of muscular activity.

Feeling that the presence of diacetic acid and acetone in the urine due to dehydration and starvation and the acidosis evidenced by blood CO_2 was in direct ratio to muscular activity, it was decided to see the effect of various sedatives.

A study of sodium amytal in eight cases showed this drug had apparently very little effect upon the blood CO_2. Three cases showed an average increase of 12.3 vol. per cent after its administration, while 5 cases showed a decrease of 11.4 vol. per cent. This indicates that

sodium amytal in moderate doses does not produce sufficient analgesia to limit muscular activity. Oftentimes patients receiving this drug are more excitable, with more muscular effort and probably this accounts for the increasing acidosis, if it can be classified as such. In a few selected cases hyoscine was given in conjunction with sodium amytal. There was a definite rise in the blood CO_2. By increasing

TABLE II. CO_2 READINGS ON 65 PATIENTS—SECOND STAGE OF LABOR

PATIENTS	READINGS	PATIENTS	READINGS	PATIENTS	READINGS
1	45.0	23	30	45	44
2	44.0	24	42	46	42
3	49.0	25	46	47	46
4	42.0	26	34	48	35
5	49.0	27	44	49	39
6	47.0	28	31	50	29
7	48.0	29	35	51	34
8	34.0	30	32	52	47
9	32.0	31	32	53	37
10	48.0	32	36	54	35
11	33.75	33	37	55	45
12	43.60	34	29	56	46
13	30.0	35	43	57	33
14	46.0	36	35	58	34
15	47.0	37	44	59	39
16	42.0	38	42	60	37
17	51.75	39	46	61	37
18	53.30	40	35	62	41
19	40.0	41	39	63	35
20	35.0	42	29	64	39
21	46.0	43	43	65	44
22	51.0	44	35		

EXPERIMENT 2. EXPERIMENTAL ALKALOSIS PRODUCED BY INTRAVENOUS SODIUM BICARBONATE

DOG	CONTROL	CONDITION OF DOG	INTRAVENOUS SOL.	TIME	2ND. CO_2	CONDITION OF DOG	INCREASE CO_2
11	42 Vol.	Ether	Soda 5 % of 15 gm.	35 Min.	238%	Died 4 hr. later. Hemolyses	196 Vol.
14	54 Vol.	No ether	Soda 5% of 15 gm.	25 Min.	238%	Died in convulsions	184 Vol.
15	46 Vol.	No ether	Soda 2% of 8 gm.	20 Min.	138%	No effect	92 Vol.
15	138 Vol.	No ether	Soda 2% of 4 gm.	15 Min.	148%	No effect	10 Vol.
1	53 Vol.	No ether	Soda 5% of 20 gm.	45 Min.	138%	No effect	85 Vol.

Sodium bicarbonate intravenously rapidly produces an alkalosis. One gram of soda elevates the CO_2 7 to 8 Vol. It likewise overcomes the acidosis produced by etherization shown in Experiment 1. Dog 11 died of alkalosis. Slowing of the respiratory function and hemolysis of the corpuscles are indicative of lethal alkalosis which has an end point of 238 Vol. per cent in dogs. Convulsions are not constant and while Dog 14 died with convulsions, Dog 11 who died had none. Venous congestion is the only apparent evidence of cardiovascular involvement. Vomiting was occasionally seen and diarrhea was a constant sign before death. It seems that a 2 per cent solution of sodium bicarbonate can be given without harmful effects, while a 5 per cent solution produces a too rapid and marked alkalosis.

pulmonary ventilation hyoscine was proved of some value, but mainly because it always intensified the sedation consequently reducing muscular activity. Sodium bicarbonate by mouth was given in a few cases with sodium amytal and hyoscine. The CO_2 was elevated from 4 to 24 vol. per cent, indicating its value as an adjunct with analgesic medication.

Pursuing our original motive, the correction of physiologic acidosis by the administration of soda, it was decided to attempt to combat the

TABLE III. POSTPARTUM CO_2 READINGS

PATIENTS	READINGS	PATIENTS	READINGS	PATIENTS	READINGS
1	36.0	18	35.3	35	55
2	57.6	19	49.3	36	65
3	51.0	20	29.2	37	48
4	34.0	21	43.0	38	63
5	86.6	22	40.0	39	50
6	36.6	23	35.0	40	65
7	56.3	24	40.0	41	50
8	38.0	25	46.0	42	63
9	52.0	26	35.0	43	42
10	50.0	27	43.0	44	45
11	50.0	28	38.0	45	47
12	48.0	29	44.0	46	51
13	48.0	30	44.0	47	53
14	62.3	31	59.0	48	55
15	46.6	32	47.0	49	42
16	53.6	33	61.0	50	57
17	51.3	34	48.0		

EXPERIMENT 3. EXPERIMENTAL ACIDOSIS PRODUCED BY INTRAVENOUS LACTIC ACID

DOG	CONTROL	CONDITION OF DOG	INTRAVENOUS SOL.	TIME	2ND CO_2	CONDITION OF DOG	DECREASE CO_2
3	56 Vol.	Normal	Lactic Acid 1%—4 gm.	40 Min.	42 Vol.	No effect	14 Vol.
3	42 Vol.	Normal	1%—3 gm.	20 Min.	50 Vol.	No effect	Increase of 8 Vol.
4	56 Vol.	Normal	2%—14 gm.	25 Min.	15 Vol.	Slow respiration	Decrease of 41 Vol.
17	46 Vol.	Normal	2%—10 gm.	30 Min.	29 Vol.	Blood slightly hemolyzed	17 Vol.
17	29 Vol.	Normal	2%—10 gm.	30 Min.	16 Vol.	Slow, deep resp.; irritability	13 Vol.
17	16 Vol.	Normal		40 Min.	16 Vol.	Marked hemolysis. Diarrhea, hemoglobinuria, vom. bl.; recovered	No change
2	50 Vol.	Normal	3%—9 gm.	20 Min.	25 Vol.	Hemolysis-Rec. Died.	25 Vol.
2	25 Vol.	Normal	3%—1.5 gm.	20 Min.	7 Vol.	Hemoglobinuria	18 Vol.

Lactic acid given intravenously produces acidosis. One gram reduces CO_2 4.3 Vol. per cent. A 3 per cent solution in the normal dog produces death. Impending signs: respiratory failure and hemoglobinuria with occasional vomiting and diarrhea. The 2 per cent solution aside from a mild hemoglobinuria is without unharmful effects. A 1 per cent solution can be used safely and produces the desired acidosis.

acidosis of labor by the administration of sodium bicarbonate. Sodium bicarbonate was given in 60 gm. doses by mouth at hourly intervals and blood CO_2 estimations recorded. There was a definite return of the CO_2 to normal in ratio to the amount of soda.

Table IV presents the blood CO_2 estimations of a series of 20 patients who were given sodium bicarbonate in dram doses by mouth during the conduct of normal labor, the dehydration and starvation acidosis having been eliminated by fluids and foods. The average blood CO_2 in two-thirds of the cases was increased 13.2 vol. per cent, while in the severe labor amounting to one-third, the total number of cases showed an average of 4.4 vol. per cent. This response to sodium bicarbonate in severe labors probably could have been overcome by pushing more medication. However,

TABLE IV. EFFECT OF SODIUM BICARBONATE ON ACIDOSIS IN LABOR

	NO. HR. OF LABOR BEFORE $NaHCO_3$	TIME FROM Na TO 2ND CO_2	1ST CO_2	2ND CO_2	INC.	DEC.
1	16′30″ PV Sev.	4 hr. (12 gm.)	37.0	49.6	12.6	
2	5′ PII Mild	4 hr. 30 min.	48.0	56.0	8.0	
3	13′30″ PI Mild	6 hr. 30 min.	53.3	61.0	7.7	
4	9′30″ PI Mild	1 hr. 50 min.	42.0	56.0	14.0	
5	12′ PI Severe	4 hr. 10 min.	41.6	43.0	1.4	
6	11′15″ P7 Sev.	3 hr. 15 min.	35.0	38.0	3.0	
7	22′ PI Mod. Sev.	9 hr.	44.0	56.6	12.6	
8	13′20″ PI Mod.	6 hr.	42.6	67.6	25.6	
9	16′ PII Severe	3 hr.	33.3	30.0		3.3
10	12′ PI Mild	8 hr.	32.0	41.0	9.0	
11	2′54″ PII Mod.	3 hr.	46.0	43.6		2.4
12	4′ PI Mod.	1 hr. 35 min.	46.0	58.0	12.0	
13	18′40″ PI Mod.	2 hr. 40 min.	40.0	52.0	12.0	
14	10′30″ PI Sev.	4 hr.	48.0	39.6		8.4
15	10′	4 hr.	34.0	56.3	22.3	
16	8′30″ PII Sev.	1 hr. 5 min.	24.0	20.6		4.0
17	2′5″ PI Mod. Sev.	3 hr. 30 min.	44.0	43.0		1.0
18	9′30″ PI Mod. Sev.	5 hr.	37.0	49.0	12.0	
19	10′	4 hr.	40.0	38.6		1.4
Aver. Approx. 12 hr.		4 hr.	40.7	53.6	13.2	4.4

EXPERIMENT 4. THE CORRECTION OF ARTIFICIALLY PRODUCED ALKALOSIS BY THE INTRAVENOUS ADMINISTRATION OF LACTIC ACID

DOG	CONTROL	ALKALOSIS PRODUCED BY	READING	CONTROLLED BY	TIME	READING	CONDITION OF DOG	DEC.
1	53 Vol.	Soda 5% of 20 gm.	138 Vol. %	Lactic acid	15	50 Vol.	Recovered Hematuria	88 Vol. %
1	50 Vol.	Totally corrected		Lactic acid 3%—12 gm.	45	34 Vol.	Recovered Hematuria	16 Vol. %
11	42 Vol.	Soda 5% of 15 gm.	238 Vol. %	Lactic acid 2%—8 gm.	25	82 Vol.	Died Hemolysis	156 Vol. %

As previously stated the end point in body economy cannot be restored as suggested in Dog 11 in which the CO_2 reached the level of 238 vol. per cent. This is beyond any clinical condition yet reported, but we were able to reduce the severe alkalosis to 82 vol. per cent. This death of the dog might result from the rapid change from one extreme to the other and as applying to patients naturally would not be encountered. In Dog 1 a mild alkalosis was produced and was neutralized with a 3 per cent solution. It was previously stated in this strength to be harmful to the normal dog, but in this extreme alkalosis it caused no damage. We are certain that a 2 per cent solution would have accomplished the desired result without risk.

TABLE V. SHOWING INADEQUATE ABSORPTION OF SODIUM BICARBONATE BY RECTUM

	NO. HR. OF LABOR BEFORE $NaHCO_3$	TIME FROM Na TO 2ND CO_2	1ST CO_2	2ND. CO_2	INC.	DEC.
	Administration per Rectum					
1	3'45" PI Mod. Sev.	3 hr. 5 min.	54.0	38.0		16.0
2	7'15" PI Mod. Sev.	10 hr.	35.3	40.0	4.7	
3	23'15" PI Mod.	3 hr.	52.0	45.3		6.7
	Aver. 11 hr. Approx.	5 hr. 20 min.	47.1	41.3	4.7	11.3
	Administration by Vein to Antepartum Cases—9 Mo. Pregnant					
1	500 c.c. 2%	1 hr. 10 min.	43.0	58.0	15.0	
2	1000 c.c. 2%	2 hr. 40 min.	48.0	65.3	15.3	
	Average	1 hr. 55 min.	45.0	60.6	15.1	

EXPERIMENT 5. CORRECTION OF ARTIFICIAL ACIDOSIS BY INTRAVENOUS SODIUM BICARBONATE SOLUTION

DOG	CONTROL	ACIDOSIS BY LACTIC ACID	TIME	READING	CORRECTED BY SODA SOL. 5%	TIME	READING	CONDITION OF DOG
2	50	9 gm. 3%	20	25 Vol.	25 gm.	15 min.	213 Vol.	Died
		1.5 gm. 3%	20	7 Vol.				
4	56	Lactic Acid 14 gm. 2%	25	15 Vol.	Soda 5% 15 gm.	20 min.	113 Vol.	Good
4	113				Soda 5% 15 gm.	25 min.	163	Diarrhea but recovered

Dog 2 records the correction of an extreme acidosis of 7 vol. per cent produced by lactic acid and was reversed to an extreme alkalosis of 213 vol. per cent. It is true the dog died, but the result is interpreted in the same manner as previous experiments. Dog 4 a moderated acidosis was corrected by a 5 per cent solution of sodium bicarbonate without any effects. It is certain that a 2 per cent solution would have accomplished the same results without the necessary risk.

EXPERIMENT 6. THE EFFECT OF AN INTRAVENOUS COMBINATION OF GLUCOSE AND SODIUM BICARBONATE. THIS EXPERIMENT WAS DONE TO PROVE THE INCOMPATIBILITY OF THESE TWO DRUGS WHEN COMBINED

DOG	CONTROL	CONDITION OF DOG	INTRAVEONUS SOL.	TIME	2ND. CO_2	END RESULTS
9	50 Vol.	Ether	Glucose 20%	$1\frac{3}{4}$ HR.	34 Vol.	Died—Bl. Sugar 606
13	45 Vol.	Starved	Glucose 20% 100 gm. Soda 2%—Insulin	50 Min.	84 Vol.	Convulsions
13	84 Vol.	Starved	Nothing	45 Min.	52 Vol.	Death
6	42 Vol.	Starved Ether	Glucose 20% 40 gm. Soda 5% 10 gm.	15 Min.	128 Vol.	
6	128 Vol.		Glucose 20% 20 gm. Soda 5 gm.	15 Min.	148 Vol.	Convulsions
6	148 Vol.		No Sol.	20 Min.	70 Vol.	Death
7	48 Vol.	Starved Ether	Glucose 20% 40 gm. Soda 10 gm.	20 Min.	113 Vol.	
7	113 Vol.	Same	Same	20 Min.	128 Vol.	Convulsions
7	128 Vol.	Same	Same	45 Min.	85 Vol.	Death

In a series of 8 dogs in which acidosis had been produced by etherization, a combination of glucose solution 20 per cent and sodium bicarbonate 5 per cent were given intravenously. Death followed in each of the 8 dogs. This corroborates our previous clinical impression that this combination is lethally toxic.

vomiting is nearly always associated with the administration of soda by mouth when given in greater doses than one dram per hour. Due to the uncertainty of action of sodium bicarbonate given intravenously before our experimental studies on dogs and knowing the unreliability of sodium bicarbonate by rectum, we hesitated to routinely prescribe its administration intravenously.

Table V shows the inadequate absorption of sodium bicarbonate per rectum. Included are three patients, two of whom were antepartum. One of these received 500 c.c. of 2 per cent solution of sodium bicarbonate intravenously with an increase in the blood CO_2 vol. of 15 per cent. The other patient received 1000 c.c. of a 2 per cent solution with an increase of 15.3 vol. per cent. No untoward reactions were observed. Substantiated by experimental observations to be reported later, we feel that it can be used if indicated with beneficial results and without damage to the organism providing its administration is controlled with CO_2 readings.

To substantiate the above clinical observation, it was thought not only advisable, but imperative to reproduce extreme states of alkalosis and acidosis in dogs in an effort to test the harmfulness and efficacy of these drastic measures suggested.

CONCLUSIONS

1. Acidosis is a frequent accompaniment of normal labor. Its severity varies in ratio to the duration and character of labor.

2. The examination of urine for acetone and diacetic acid is indicated in every case. These probably result from starvation and dehydration and can be eliminated by fluids and food. The association of acidosis revealed by CO_2 determination in the absence of acetone and diacetic acid in the urine is due to the accumulation of lactic acid resulting from muscular activity. Sedatives apparently lessen this acidosis by diminishing muscular activities.

3. A CO_2 determination is indicated in prolonged or exhaustive labor. Past CO_2 determinations on such cases revealed a marked acidosis and should be corrected if present before an anesthetic or an operative procedure is begun.

4. Experimental acidosis can be produced by the administration of intravenous lactic acid.

5. Experimental alkalosis can be produced rapidly by the intravenous administration of sodium bicarbonate.

6. Severe acidosis in the dog was corrected by a 2 per cent solution of sodium bicarbonate without ill effects.

7. Experimental alkalosis in the dog was corrected by a 2 per cent solution of lactic acid. A 1 per cent solution proved to be the proper solution to correct this condition.

8. The extreme alkali-acid imbalances in the dog are therefore correctable.

9. Our experimental correction of alkalosis and acidosis in the dog bids to be a valuable adjunct in resuscitating exhausted patients in labor that have frequently heretofore died.

10. Verification of the experimental evidence remains to be proved in the near future in clinical cases of the extreme types.

WEIGHT CHANGES IN PREGNANCY*

PHILIP N. BRAY, M.D., DULUTH, MINN.

INTRODUCTION

VARIOUS research workers, especially Cummings,[1] have come to the conclusion that weight changes in pregnancy have a definite relationship to obstetric pathology. Hence this study of weight changes in normal pregnancies was undertaken: (1) To determine whether or not parity, age, and body build are factors in the changes in body weight during pregnancy and the puerperium. (2) To determine whether or not the daily weight changes in the first eight days postpartum are all decreases, whether or not there are any significant differences in them, and if there are significant differences on which days they occur. (3) To determine the total amount of weight change in the first eight days postpartum.

SUMMARY OF THE LITERATURE

In summarizing the literature on the subject, it becomes evident that conflicting results have been obtained from the time of Gassner's[2] work in 1862. Most workers have thought that parity, body build, and age all affect weight changes in the prenatal and puerperal periods. However, there is considerable variation of opinion on the type and amount of puerperal weight changes. This review of previous work was given in absolute weight changes rather than relative.

The literature on the prenatal period will be analyzed first. The following men, Gassner[2] (1862), Baumm[3] (1887), Lorenzen[4] (1921), Kemper[5] (1924), DeLee[6] (1928), and Trillat[7] (1928) came to the conclusion that multiparae gained more than primiparae; while Hannah[8] (1925) and Cummings[1] (1934) found that primiparae gained more than multiparae. Zangemeister[9] (1916) found that multiparae and primiparae increased in weight equally from the 29th week on. Siddall and Mack[10] (1933) found that parity had little, if any, influence on the weight changes. The following men, Gassner[2] (1862), Baumm[3] (1887), Zangemeister[9] (1916), Lorenzen[4] (1921), Kemper[5] (1924), Mahnert[11] (1924), and Kerwin[12] (1926) found that heavy women gained more than light. None of the work showed the reverse, that the light women gained more than the heavy. Siddall and Mack[10] (1933) came to the conclusion that body build had little, if any, influence in weight changes. The following workers, Lorenzen[4] (1921), Kemper[5] (1924), and Siddall and Mack[10] (1933) found that the young women gained more than the old. None of the workers were of the opposite opinion, that the old women gained more than the young.

Next the literature on the puerperal period will be analyzed. The following men, Gassner[2] (1862), Baumm[3] (1887), and DeLee[6] (1928) came to the conclusion

*This study was submitted to the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Obstetrics and Gynecology.

that multiparae lost more than primiparae. The reverse, that primiparae lost more than multiparae, was found in one phase of Kemper's[5] work (1924). Heil[13] (1896) found that para i, iii, iv, and v lost less than the average, while para ii lost more than the average. The following, Gassner[2] (1862), Baumm[3] (1887), Heil[13] (1896), and DeLee[6] (1928) came to the conclusion that heavy women lost more than light. The reverse, that light women lost more than heavy, was found in one phase of Kemper's[5] work (1924). In comparing the weight changes between old and young in the puerperium, Heil[13] (1896) found that in the youngest and oldest groups, the weight loss was under the average. Kemper[5] (1924) found a great diversity of results according to what groups were compared. First, he analyzed the first twelve puerperal days. He found in comparing the heavy elderly multiparae and the light young primiparae, that the heavy lost more than the light, the elderly more than the young, and the multiparae more than the primiparae. In comparing the heavy young multiparae and the light old primiparae he found, also, that the heavy lost more than the light, the old more than the young, and the multiparae more than the primiparae. However, he found that heavy old multiparae lost more than light old multiparae, the light old primiparae lost more than heavy old primiparae, the heavy young multiparae lost more than light young multiparae, and heavy young primiparae lost more than the light young primiparae. When Kemper[5] compared the weight losses of delivery plus the first twelve puerperal days, he found the heavy lost more than the light, the old more than the young, and the primiparae more than the multiparae.

Gassner[2] (1862), Baumm[3] (1887), and Heil[13] (1896) were the only authors who stated whether or not the immediate puerperal weight changes were all decreases. Gassner[2] (1862) and Baumm[3] (1887) found the puerperal weight changes to be all decreases. Gassner[2] (1862) carried his figures through the eighth day postpartum and Baumm[3] through the sixth day postpartum. Heil[13] (1896) found from the eighth postpartum day on there was an increase until the thirteenth day, when he discharged his patients. (He frequently had a very small secondary reduction on the ninth, tenth, or eleventh day.)

Significant differences in the daily puerperal weight changes were shown in the work of Gassner[2] (1862), Baumm[3] (1887), and Heil[13] (1896). Heil[13] (1896) found a definite augmentation of loss on the first, fifth, and sixth days. Gassner[2] (1862) found a definite augmentation of loss on the first day, then a more or less gradual diminishing loss. Baumm[3] (1887) found a definite augmentation of loss on the first and fourth days, with a gradual increasing loss on the fifth and sixth days.

The total amount of weight change in the immediate puerperium of the various authors, will next be analyzed. Gassner[2] (1862) found a loss of 4.868 kilograms in eight days. Heil[13] (1896) found a loss of 1.700 kilograms in eight days. Zangemeister[9] (1916) found a loss of 1.61 kilograms in seven to twelve days. Kemper[5] (1924) found a loss of 1.261 kilograms in twelve days.

From this review and summary it becomes apparent that there is: (1) only a small amount of previous work, (2) a great conglomeration of conflicting ideas and opinions as to the effect of pregnancy and the puerperal state on the weight of women, (3) a complete lack of sufficiently accurate work to measure small changes in weight correctly, and (4) a complete lack of statistical evaluation of the weight changes.

METHOD OF COLLECTING AND ANALYZING DATA

Since the purpose of this study was to measure the physiologic changes in body weight of women during the prenatal and puerperal periods, care was taken to exclude all cases of toxemia, abnormal de-

livery, and febrile puerperium. As a starting point in the weight history the patients stated their normal nonpregnant weight, wearing their usual house clothes. Usually the patients had been weighed within a short time before they became pregnant.* During the prenatal period the patients were weighed with clothes on every two weeks until the last month, and every week during the final month. These prenatal weighings were done on the usual pound and ounce lever scale, and the results converted into kilograms.

The weighings just before delivery and during the puerperium were taken on a very delicate Henry Troemner scale. This scale was graded in the metric system, and was constructed like the instruments used in quantitative chemistry. The scale guarantee was that of a sensitivity of plus or minus 5 gm. with a load under 300 pounds. Actually, however, it was found to be more sensitive than this, as changes down to a gram were registered.

One woman was weighed at a time. A wheel litter was used in transporting the patient to the scale. The top of the litter was detachable from the four-wheel frame. Four chains were hung from one end of the scale bar, and these snapped onto the litter top. This top, a blanket, and a perineal pad were first carefully balanced to zero by means of a bucket of fine lead shot hung from the other end of the scale lever bar. The patient was then placed on the litter top, wearing the perineal pad, and covered only by the blanket. The litter frame was pushed away, so that the actual weighing was only of the patient, as everything else had been previously balanced to zero. The method of weighing was the same as that used in quantitative chemistry, taking a certain number of oscillations, averaging and finding the dead center.

Sixty-nine women were weighed on this accurate scale just before delivery, immediately after delivery, and at the same time each afternoon during their hospital stay. They were given a thorough enema before delivery, and their bowels were kept open after delivery. Five of the women, however, insisted on going home on the seventh postpartum day, so that only 64 cases were completed. All component products of labor were weighed on a smaller metric lever scale. The products consisted of fetus, placenta, fetal urine and stool, mother's urine and stool, and blood (a small additional remainder of the blood had to be estimated). The remaining difference between predelivery and immediate postdelivery weight covered amniotic fluid and moisture lost by skin evaporation and respiration of mother.

*I gained the impression that the patients were not guessing as to their weight, but had been weighed within a month or so before becoming pregnant. This means that the weights were probably accurate within the limits of ordinary commercial scales which are found in grocery stores and drug stores.

For purposes of comparison and study, the basic data were divided into a number of groups.

The first division was according to parity, first into three groups: para i, para ii, para iii and over, and second into primiparae (para i) and multiparae (para ii and over).

The second division was according to three age groups, young less than twenty-five years, medium twenty-five years to thirty-five years, and old over thirty-five years.

The third division was according to three groups of body build: slender, medium, and stout. The slender group included all women under two pounds per inch of height, medium from two pounds to 2½ pounds per inch of height, and stout all cases of 2½ pounds and over per inch of height. Since there were only 5 cases in the stout group subsequent comparisons were limited to those between the slender and the medium groups. Also, since there were only one slender and one medium weight woman over thirty-five years, these two cases were omitted. Consequently, the weight comparisons in this group were made up of women in the slender and medium weight groups, under thirty-five years of age.

The mean weights and their standard errors were computed by the usual statistical methods for each one of these subgroups. The difference between any two means was tested for significance by the ratio of the difference to its standard error, that being the commonly used relative deviate.

When R is 2.0, such a difference between two means would occur for two samples from the same population only 5 in 100 times. When R is 3.0, such a difference would occur between two samples from the same population only 1 in 100 times. According to common statistical practice a difference is considered significant when it would not occur by chance oftener than 1 in 100 times, i.e., when R is 3 or more. Some workers consider a R of 2.0 as indicating a possibly significant difference. Since P, the probability integral, indicates the chances in unity, P times 100 equals the chances in 100. The means for the various groups are given in Charts 1 to 5.

RESULTS

According to the figures in Chart 1, parity makes no difference in the increase in body weight of pregnant women, since in this series none of the differences between the means had relative deviates as large as 2.0. Similar analyses showed the same lack of difference in prenatal increase in weight for age and body build. The chart shows that the mean increase in weight during pregnancy is 10,750 kilograms. Too much reliance cannot be placed on this figure because of the unknown sources of error in the measurement of preconception weight of the women.

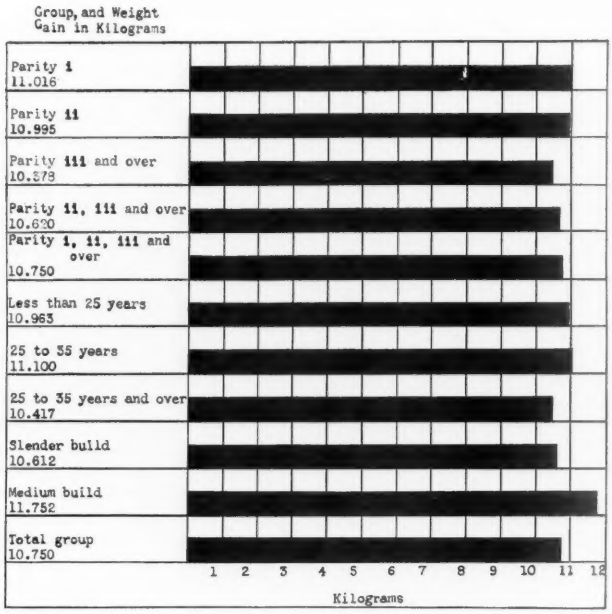
Group, and Weight Gain in Kilograms
Parity 1 11.016
Parity 11 10.995
Parity 111 and over 10.378
Parity 11, 111 and over 10.630
Parity 1, 11, 111 and over 10.750
Less than 25 years 10.963
25 to 35 years 11.100
25 to 35 years and over 10.417
Slender build 10.612
Medium build 11.752
Total group 10.750
1 2 3 4 5 6 7 8 9 10 11 12
Kilograms

Chart 1.—Graph made of the means of the total weight gains in kilograms during the prenatal period.

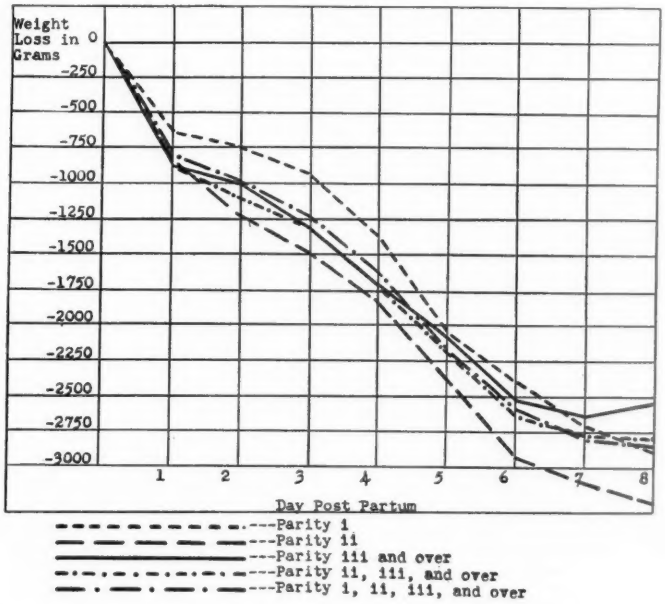

Chart 2.—Graph made of the means of the daily weight losses in grams during the first eight days postpartum according to parity. *O*, the first (immediate) postpartum weight.

According to the values given in Chart 2, parity makes no difference in the changes in mean daily weight during the puerperal period, since none of the differences between means for the same day had relative deviates of 3 or more. (There were three differences that had a relative deviate between 2 and 3, but all the rest were less than two.)

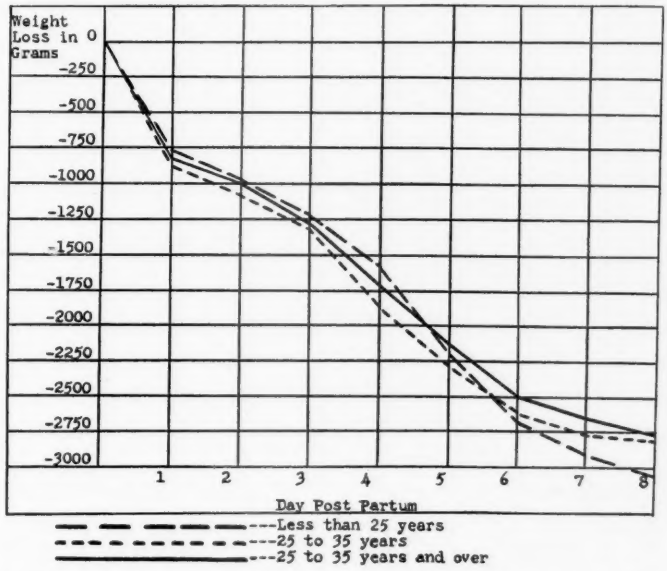

Chart 3.—Graph made of the means of the daily weight losses in grams during the first eight days postpartum according to age. *O*, the first (immediate) postpartum weight.

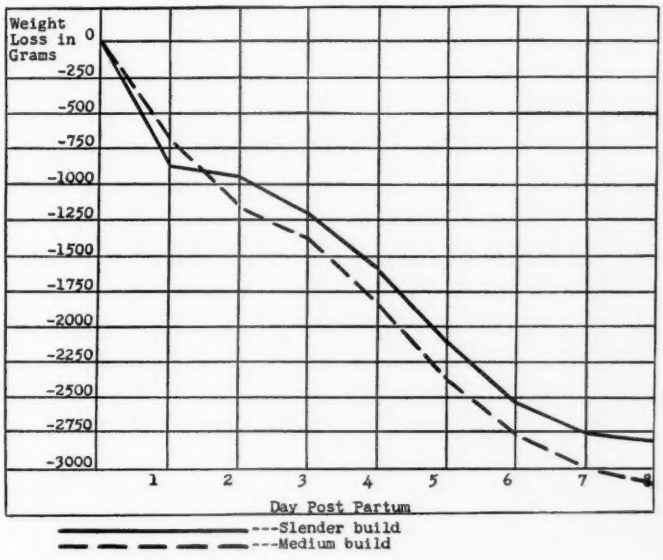

Chart 4.—Graph made of the means of the daily weight losses in grams during the first eight days postpartum according to body build. *O*, the first (immediate) postpartum weight.

Likewise, age does not affect the daily postpartum changes in weight (Chart 3), as none of the differences between the means for the same day in the age groups had relative deviates as large as 2.

With body build only one difference between the mean daily weight changes for slender and medium build (Chart 4) had a relative deviate between 2 and 3, all others being less than 2. Therefore, body build also had no influence on postpartum decrease in weight.

The mean daily weight changes of the whole group for the first eight puerperal days were next compared to each other as shown in Chart 5. These changes show that they are all decreases. The decrease for the first day is significantly greater than that for any other day with the

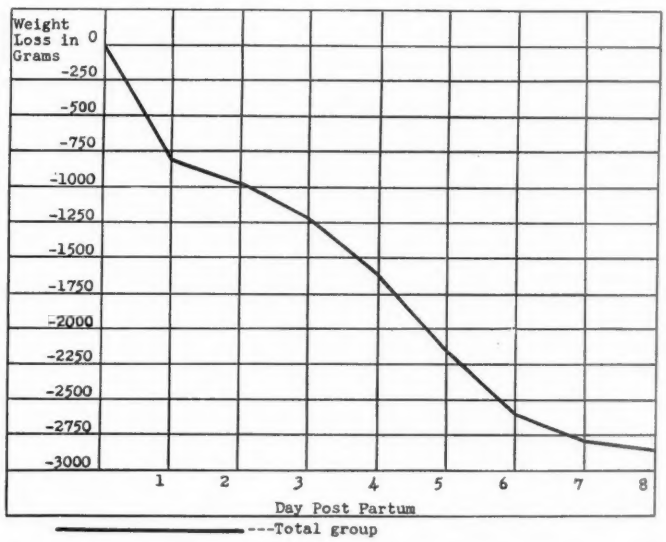

Chart 5.—Summary graph made of the means of all the cases.

possible exception of the fifth day, when the relative deviate of 2.7 indicates a possibly significant difference. Also, the decrease for the fifth day tends to be significantly greater than that for all days except the two adjacent ones, the fourth and sixth. These differences indicate that the postpartum decrease in weight is not regular, but instead is largest (0.8 kilo.) on the first day, drops to 0.2 kilogram on the second day, then increases to 0.5 kilo. by the fifth day, and decreases again to the low level of 0.06 kilo. on the eighth day. The significance of the differences between the decrease for the first and other days, and between the fifth and most other days, indicated that there is a true augmentation of the postpartum decrease on the first and fifth days.

The total amount of decrease in weight for the whole group in the first eight puerperal days was 2.831 kilo. ± 0.140 kilo.

DISCUSSION

This statistical analysis of new data has failed to substantiate earlier opinions that parity, age, or body build has an effect upon the increase of weight during pregnancy and the decrease of weight in the puerperium. Only Siddall and Mack[10] have found similar negative results as to the effect of parity and body build, and Zangemeister[9] as to the effect of parity on weight variations in the prenatal period. However, Siddall and Mack[10] did think that age was a factor, the younger women gaining more than the older.

There has been a tendency, similar to the findings in this analysis, to note the major decrease in weight in the puerperium on the first and fifth or one of the two adjacent days. As previously stated, Heil[13] found an augmentation of loss on the first, fifth, and sixth days, Gassner[2] on the first day, and Baumm[3] on the first and fourth days with a gradual increasing loss on the fifth and sixth days.

The total decrease in weight in the first eight days of 2.831 kilo. ± 0.140 kilo. in this study falls intermediate between the low value of 1.700 kilo. found by Heil[13] and the high value of 4.868 kilo. found by Gassner.[2] Obviously, the amount of decrease would be materially affected by differences in diet and management of puerperium.

SUMMARY AND CONCLUSIONS

1. Parity, age, and body build are not factors in the changes in body weight of women during the prenatal period and the first eight days of the puerperium.

2. The daily weight changes during the first eight puerperal days are all decreases, there being significant augmentations of loss on the first and fifth days.

3. The total mean weight loss in the first eight puerperal days is 2.831 kilo. ± 0.140 kilo.

I am indebted to Dr. Jennings C. Litzenberg and Dr. John A. Urner of the Department of Obstetrics and Gynecology for advice concerning the problem, and to Dr. Edith Boyd of the Department of Anatomy for assistance in statistical analysis.

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WHEAT GERM OIL THERAPY

III. Rat Experiments, Lactation, Clinical Uses, "Failures," and Effect Upon Congenital Anomalies

Evan Shute, B.A., M.B., F.R.C.S.C., London, Canada

(From the Department of Obstetrics and Gynecology, University of Western Ontario)

RAT EXPERIMENTS

As was mentioned in a previous publication,[1] female rats fed on an E-free diet developed in two to four months the classical evidences of E-deficiency, viz., the habit of resorbing their fetuses. At the same time their blood serum revealed the presence of the antiproteolytic estrogenic factor for the first time. On the other hand, in normal control rats this was not the case. That report indicated that 88 per cent of a group of 16 rats showing sufficient deficiency of vitamin E to cause all their fetuses to be resorbed revealed the presence in their sera of this antiproteolytic power, whereas only 5 per cent of a group of 20 rats given vitamin E or fed on approximately normal diets, or on E-defective diets for too short a time to become E-free, or normally fed male rats, revealed such power. Since that paper appeared, we have tested more rats under the same circumstances and now can report that our total figures should be respectively 93 per cent of a group of 30 rats and 11 per cent of a group of 28 rats. The accuracy of the test is well illustrated by these figures.

LACTATION

Another feature of interest is the fact that 16 of our 60 patients, who during pregnancy displayed an excess of the estrogenic antiproteolytic substance in the blood, and required wheat germ oil in order to reach term, had an unusual amount of milk secretion just after delivery. One primiparous patient had 8 ounces of milk available for each nursing for days, and another primipara easily produced 7 ounces or more for each nursing. Another primiparous woman had so much secretion on the day after delivery that she soaked her clothing and bed, as a few women do on the fifth to tenth days postpartum. Surprisingly enough, we have noticed no tendency for this exaggerated milk secretion to continue beyond the first seven to ten days postpartum. Indeed, after that time five of these 16 women experienced genuine difficulty in providing adequate quantities of breast milk for their infants. On the other hand, 5 of our patients treated with the oil throughout pregnancy had a

minimal amount of lactation from the very beginning, drying up before the third day. To sum up, 36, or 60 per cent, of the 60 patients treated with wheat germ oil during their pregnancies were able to nurse their babies for three months or longer, and 5 had very defective lactation from the first. Sixteen, or 27 per cent, at the beginning exhibited an unusual amount of secretion. As a control series we may refer to the nursing records of our last 60 patients who carried pregnancies to term without the use of wheat germ oil. Thirty-five, or 58 per cent, of the 60 were able to nurse their babies, and 18 had very poor lactation from the very beginning. Only 7 exhibited evidences of an unusually large amount of milk secretion.

It is known, of course, that estrin is responsible for nipple development and the proliferation of the duct system of the breasts. The mammatropic hormone from the anterior lobe of the pituitary gland, which is directly responsible for milk secretion, comes into full play when the estrin of the body has been excreted in the puerperium, and this is supposed to be fairly complete by ten days, or even sooner.

Sure[2] showed that rats kept on a diet deficient in reproductive vitamins, but bred so soon after being put on this diet that they could deliver live young, could rear these up to the fifteenth or seventeenth day of life. Then lactation suddenly became inadequate and the young reached a weight plateau and soon perished. The administration of wheat germ oil to the mother rats, however, soon enabled lactation to proceed adequately and many young were saved. He believes the lactating mothers had depleted their reserves of the lactation-promoting fraction of vitamin E and required the ingestion of more before further nursing could be accomplished. Later[3] he indicated that both the antineuritic and growth-promoting fractions of vitamin B are important for adequate lactation in rats. With this work of Sure's in mind, we have tried large doses of wheat germ oil in the effort to stimulate lactation in 23 women in the puerperium. All were patients who could not produce more than 4 ounces of milk per day in spite of every effort that could be made. Fifteen of the 23 had taken wheat germ oil during their pregnancies. Of these 10 patients we were successful in inducing adequate lactation in 6 and failed completely in 9. Of the other 8 we had success with 2. Altogether the successes were 8 in 23 cases, or roughly 35 per cent.

The patients who were successfully treated thus for inadequate lactation reported definite tingling of the breasts appearing in about five or six hours after the administration of an ounce of the oil. The breasts were well filled with milk before twenty-four hours had elapsed, but treatment had to be kept up for about two weeks on the average. If it were stopped, lactation ceased, only to start up just as before when the oil was taken again. Sure remarked that rats required about twice as much oil for lactation as for reproduction, but this did not appear to be true in this small group of women we have studied.

The number of our cases is too small to warrant any inferences, except that it seems as if a brief trial with a large dose of wheat germ oil might be indicated in those women who evince defective lactation in the puerperium.

CLINICAL USES

Should every pregnant woman take wheat germ oil? One suspects the answer should be in the affirmative. It has long been recognized that a very high percentage of pregnancies in both America and Europe terminate prematurely, whether by act of nature or human intervention. It would appear that the greater proportion of these abortions are natural, for the success of widely known abortifacient medicines taken orally and known by the whole profession to be inert, suggests that abortion was impending when these drugs were taken and that their success was largely a triumph of coincidence. If we were to admit that even one-tenth of conceptions were in danger of premature spontaneous interruption, the widespread use of wheat germ oil early in gestation might seem to be justified. If, however, there be added to this indication for its use the beneficial effects achieved by it in the prophylaxis and therapy of abruptio placentae,[4] and if that complication of pregnancy occurs as commonly as Goodall would have us believe,[5] and as I also feel,[6] then there is some reason to advise the use of vitamin E therapy in every pregnancy. In the past four years I have had no habitual aborters in my private practice, but have treated 12 miscarriages and 17 abortions with wheat germ oil. Miscarriage was prevented in 91 per cent and abortion in 88 per cent of the group of patients so treated. The therapeutic success with the whole group of 29 cases therefore averaged 89 per cent.

The effect of the oil in stimulating defective lactation in a certain percentage of women has been indicated earlier in this paper.

If it is true that vitamin E acts largely through its antagonism to estrogenic substances in the blood, then it should have a place in the therapeutic fields now occupied by pregnancy urine gonadotropic hormone, thyroid extract and progesterone. In a previous paper[7] we suggested that it might be of use in treating defective male patients, as had been suggested earlier by Moench.[8] We produced testicular descent in a boy by means of its use after a long trial with a pregnancy urine gonadotropic substance had failed to help. We have used it successfully in a very small number of cases of dysmenorrhea which were associated with a high blood content of estrogenic substance, based on the analogy between its action and that of progesterone. Vaginal and anal pruritus[9] have been helped by it in women whose blood showed estrin excess.

One does not feel that its usefulness as a therapeutic agent has been exhausted by any such list as the above. Undoubtedly many more pathologic entities will be found to be associated with an excess of estrogenic material in the blood, and will be materially helped by therapy directed toward the correction of such excess.

FAILURES WITH WHEAT GERM OIL THERAPY

From what has gone before, it can be seen that many of the failures with wheat germ oil therapy have their origin in factors which are readily controllable. That there is a considerable percentage of failures cannot be denied.

Vogt-Möller[10] in his series of 23 cases reported that 78 per cent of the patients went to term and 87 per cent delivered viable children. Watson and Tew[11] in 53 cases reported 72 per cent success. More recently Currie[12] has reported 86 per cent of his 35 cases carried successfully to term or beyond the fifth month at the time his report was sent to press. Nicholson in discussing his paper mentioned that two patients whom she had treated had not had a successful outcome. The author in a series of 44 cases of spontaneous abortion[13] (as well ascertained as such cases can ever be) and 26 cases of spontaneous miscarriage[14] found in the whole group 74 per cent which showed E-deficiency or excess of the antiproteolytic estrogenic factor in the blood serum. As stated earlier in this paper, the author has treated 29 patients with threatened abortion or miscarriage with wheat germ oil with 89 per cent successful outcome at term. There still remains a considerable percentage of cases, ranging from 28 to 11 per cent, in which vitamin E therapy has appeared to be inadequate, but one suspects this should not constitute more than 15 per cent.

As has been indicated, failure with this mode of therapy may be ascribed to inadequate dosage, personal idiosyncrasies leading to inadequate assimilation, associated hypothyroidism, failure to allow for seasonal depletion of the body depots of vitamin E, rancid oil which has been kept at too high a temperature or allowed to deteriorate with age. Of course, we must add the very important and obvious fact that many abortions may not be due to E-deficiency or excess of estrogenic antiproteolytic substance in the blood at all, but to other factors such as infection, trauma, sperm abnormality, etc.

Once our patients are under control with wheat germ oil we allow them to take long automobile rides or do heavy work without regard to the previous precarious character of the pregnancy. We have never had any untoward results from this practice. Indeed one of our women with a threatened abortion, which was controlled by a massive dose of wheat germ oil, slipped on the stairs and descended a flight of four steps, sitting heavily on each step in doing so. There was not the slightest trace of a relapse in her condition and she had a normal delivery at term. Another case of partial abruptio placentae at the fifth month of pregnancy had her pain promptly controlled by two massive doses of wheat germ oil. On the next day she was cystoscoped for a complicating pyelitis, and did not abort.

We suspect that the reverse is also true, viz., that many of the causes of abortion and miscarriage commonly accepted as such are of only secondary importance and could never provoke a threatened or actual interruption of pregnancy unless there was a background of deficiency of vitamin E. We have repeatedly found such a deficiency in the blood sera of women who had used ridiculously ineffectual measures to induce

abortion or who had taken absurd draughts for the same purpose and been pleased by their success. Indeed Tate[15] has recently reported obtaining in the blood of a criminally aborting woman the same findings as in those of women who abort spontaneously, and which strongly suggest an excess of estrogenic substance. Mall[16] years ago observed that only one of 82 cases of abortion, from which specimens were sent to him and which were found to be so deformed that abortion was very likely, did not give a history of intervention to induce the abortion. Mall and Meyer observed that abortions ascribed to influenzal and other infections "remind one of the defective fruit which persists insecurely upon the tree until a sudden gust of wind showers it to the ground." We suspect that such factors are in great part of secondary importance, and would be ineffective if the patient were saturated and controlled properly with vitamin E.

To indicate the trend in recent opinion one may point to the work of Moussu[17] who has had considerable success in prophylactically treating endemic abortion in cattle, formerly ascribed almost exclusively to infection with *Bacillus abortus*, by means of wheat germ oil.

The author has had six instances of failure among his own patients including three premature deliveries of live children. One of these failures is included in the Watson and Tew report. In this case the blood serum was normally digestible at the time of the premature delivery. One patient aborted at the second month whose blood serum did not show any evidence of deficiency of vitamin E and on whom wheat germ oil therapy had no effect that could be discerned. The decidual cast strongly suggested that there had been an attempt at the formation of a placenta previa. In the other four cases the blood serum showed evidence of E-deficiency at delivery, however. In one of these four the patient had neglected to take her wheat germ oil for three days before she suddenly went into labor. One patient had been deliberately taken off the oil in June of 1936 and put on a green diet in the hope it might prove to be an adequate substitute. Before the mistake could be rectified her membranes had ruptured and she had gone into premature labor. In the other two cases the wheat germ oil used was very old and had become slightly rancid. In these last four cases the antiproteolytic factor had re-appeared in the blood serum at the time they went into premature labor. This is at least a very striking coincidence.

The literature would suggest that lettuce, spinach, water cress, and other such green foods rich in vitamin E can be used as a substitute for the latter when plentiful. That can be true only to a very limited extent. The author each spring and early summer for three years has attempted just such a substitution and been compelled to admit failure. Some of his patients, as has been mentioned, went into labor prematurely, and others threatened to do so. All of them showed a return of the antiproteolytic estrogenic factor in the blood in the course of a week or so

after the oil therapy had ceased. Probably so much of this estrogenic substance is in circulation in these precarious cases that a great deal of a concentrated form of vitamin E, viz., wheat germ oil, is required to prevent it from harming the pregnancy.

EFFECT UPON CONGENITAL ANOMALIES

It has long been recognized that many spontaneous abortions and miscarriages are associated with developmental anomalies of the fetus. This was best illustrated in the extensive studies of Mall and Meyer[16] at the Carnegie Institute.

Beckwith Whitehouse[18] mentioned two instances of deformed infants born at term after abortion had been averted. Moench[8] states that it is often not worth while to try to save the products of gestation nature is trying to get rid of, on account of the chance that the child will show developmental defects at birth. Mall and Meyer quoted a remark of Bacon who said he had delayed an abortion in two or three instances in which a monster had been delivered at term. Nageotte-Wilbouchewitch[19] reported two examples of threatened abortions which were carried to term only to produce idiots, and two threatened miscarriages which when carried to term or near term produced respectively an infant with a malformed chest and one with a congenital scoliosis. Kane,[20] among thirty-six living children whose mothers were habitual aborters, found that five were congenitally defective, and thought that the prevention of abortion in the early months of pregnancy merely prevented nature's elimination of the unfit. He suggested that fetal anomalies might be due to hormonal deficiency.

Some people may feel, therefore, that the prevention of abortion and miscarriage by means of adequate wheat germ oil therapy is a misdirected effort.

Falls,[21] however, using progesterone therapy was able to carry 83 per cent of his group of 41 cases of threatened or habitual abortion to viability. All that were carried to term were normal, but two of his failures were cases in which abnormal fetuses were expelled. Currie[12] carried 21 cases of habitual abortion to term with wheat germ oil therapy and notes that one of these died of a "structural deformity of the throat." Whitehouse[18] mentions a woman delivered prematurely of a spina bifida in her second pregnancy, who was carried to term in her third pregnancy by means of wheat germ oil. The normal baby delivered in this third pregnancy was born with a dimple over the lower spine. Neither Vogt-Möller,[10] Juhasz-Schaffer[22] nor Watson and Tew[11] have reported fetal anomalies in the infants brought to term by them under the influence of wheat germ oil. Of the 29 cases of threatened abortion or miscarriage carried to term on wheat germ oil by the author, one infant developed soon after birth a mild type of spasticity of the legs, which has persisted. This patient had no oil until the fifth month. Another woman, who was first seen at the fourth month with so much amniotic fluid that the fundus uteri was at the level usual for six months, was put upon wheat germ oil at the fifth month, carried thus for two months, then x-rayed. As a deformed child was detected, labor was induced and a fetus with craniorrhachischisis was delivered.

It is obvious, of course, that the prime desiderata in this problem are a means of detecting fetal anomalies before at least the twelfth week of pregnancy and a means of correcting certain types of developmental de-

fects such as spina bifida or hairlip, while the fetus is still plastic and one can hope that correction is at least theoretically possible. We do not propose to enter into any detailed discussion of these two points in this paper. Our views will be published later in more detail.

However, one can often detect spontaneous abortion before it develops by means of the author's test for a disturbance of the relation between vitamin E and estrogenic substance in the blood serum. In the hope that some success would attend a study of this equilibrium in those pregnancies which later delivered deformed infants, we tested a large number of blood samples taken in the first trimester of pregnancy, especially from women who had had anomalous fetuses previously. Our series is small, but is presented for what suggestive value it may have.

Five women who later delivered deformed infants were tested in the first trimester of pregnancy. All showed estrogenic excess and deficiency of vitamin E in their blood sera. Six out of 8 (or 75 per cent) of defective pregnancies first tested in the second trimester showed the same result. In short, where such a disturbance in the relation of vitamin E to estrogenic substance is found, one may suspect, at least, that the fetus is deformed. That deficiency of vitamin E is a factor in producing fetal deformity is strongly suggested by the studies of Macomber[23] and Byerly and his coworkers.[24] That vitamin B_1 is also a factor appears from the report of Slonaker,[25] and that estrogenic substance is involved is indicated by Kozelka and Gallagher.[26]

What will wheat germ oil, rich in both E and B_1, accomplish if given very early in pregnancy in cases in which there is marked probability that the fetus is abnormal? He would be bold who would presume to answer that question with assurance. A colleague, Dr. A. E. Mowry, had a patient whose only conceptions had resulted in two successive anencephalic infants. Before the third conception and throughout the whole of that pregnancy she was given enough wheat germ oil to control the estrogenic substance in the blood. She delivered a normal child at term. Murphy[27] has pointed out that where there is one defective child, the next child has twenty-four times as much chance of being deformed as a child chosen at random in the general population. With the background of two identical deformities in the siblings, the chance of this third conception having a normal outcome must have been very small indeed.*

There is an unusually marked tendency for harelip to be repeated in siblings, it is believed. The author had a patient whose first conception ended in a very severe cleft-palate and harelip at term. As soon as she conceived again, her blood was found to be defective in vitamin E and

*Through the courtesy of Dr. A. Sinclair of Sebringville, Ontario, I can present the report of a patient who had had in her first two pregnancies a seven-month hydrocephalic fetus and a full-term spina bifida, respectively. She was first seen by him at the sixth week of her third pregnancy and promptly put on wheat germ oil therapy. She delivered a normal child at term.

The author reported in a previous paper[1] the appearance of two hydrocephalics in the litters of his E-defective rats. Recently Barrie has confirmed and extended this observation independently. (Nature 139: 286, 1937.)

high in estrogenic substance. She was promptly put on wheat germ oil, and had an uneventful pregnancy and normal child at term.

A patient of ours, who showed all the classical signs of partial abruptio placentae in the sixth month of her first pregnancy, was carried to term on wheat germ oil. She delivered a baby that appeared to be typically Mongolian. Yet the baby appears to have normal or better than normal intelligence. It is now twelve months old.

Enough has been said, perhaps, to indicate an approach to the problem of congenital anomaly in the human being that offers some hope. At least it indicates a fertile field for further study.

SUMMARY

1. Ninety-three per cent of 30 rats kept on a diet defective in vitamin E until they began to resorb their fetuses possessed antiproteolytic power in their blood serum. Only 11 per cent of 28 rats on normal diets revealed this substance.

2. In 35 per cent of 23 women whose lactation was inadequate during the puerperium, wheat germ oil therapy restored efficient lactation.

3. Some of the therapeutic possibilities of wheat germ oil are indicated.

4. About 15 per cent of abortions are not controlled by wheat germ oil therapy. Failures are discussed.

5. As so many aborted fetuses are deformed, the question arises as to the advisability of wheat germ oil therapy designed to prevent abortion. Statistics are reviewed, and personal experiences recorded, to indicate that such therapy is probably justified.

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EPILEPSY AND PREGNANCY

A Review of the Literature and a Study of Thirty-Seven Cases

Arthur Baptisti, Jr., B.A., M.D., Baltimore, Md.
(From the Obstetrical Division of the Baltimore City Hospitals.)

THE relationship between epilepsy and pregnancy is of interest to the obstetrician from three separate angles. First, does the disease influence the course of the pregnancy in any way, and vice versa; second, what are the probabilities of the transmission of this affliction to the offspring; and third, what are the means for differential diagnosis between an epileptic seizure and an eclamptic convulsion? References to this problem are rather difficult to find in medical literature and available references for the most part consist of statements of opinion without statistical study.

The admission of a pregnant epileptic patient to the Baltimore City Hospital Obstetrical service aroused considerable interest in this problem from the viewpoint of the obstetrician. The paucity of information in the literature and the inconsistency and inadequacy of the published opinions are somewhat discouraging, and thus it seems appropriate to study the problem thoroughly with hope of throwing some light on this question, particularly of how the obstetrician may best serve the interests of his epileptic patient. This was attempted by first reviewing the literature to date and then by studying all the available case histories of epilepties in the files of the three largest obstetric clinics in Baltimore.

The first observer to mention the relationship between epilepsy and pregnancy was Echeverria, a student of epilepsy, who in 1867 published a treatise on this disease in which he stated that his general impression was that gestation usually has a favorable influence on the frequency of the epileptic fits but he gives no statistics. It is interesting and important that in those days the criteria for the presence of epilepsy in the family background were very inaccurate, and the following list represents the conditions which when found in the family history were considered positive evidence of an hereditary background: hysteria, neurasthenia, insanity, migraine, obsessions, tic, stuttering, temper, periodic headache, tuberculosis, chorea, bilious attacks, morphinism. E. M. Bridge has recently pointed out that such a miscellaneous assortment of diseases obviously is an extremely inaccurate criterion to use in a series of statistics to establish the transmission of epilepsy. In 1885 Reynolds, another student of epilepsy, reported a statistical study on 1,450 cases from the National Hospital of Paralyzed and Epileptic and found that in this series there were 785 female cases and in 7 of these cases the first fit occurred during pregnancy and in 5 others the first convulsion was observed a very short while after delivery.

The first pertinent reference to the effect of pregnancy on epilepsy appears in the German literature in 1889 when Nerlinger in a dissertation at Strassburg stated that 50 per cent of epileptics are improved by pregnancy but no statistics are offered to support this contention. In 1901 Gowers published a series of statistics which comprised 3,000 cases of epilepsy, 52 per cent of which were females and he reported that in 10 of these cases the initial attack of epilepsy occurred during a pregnancy. Hirst in the *American Textbook of Obstetrics*, published in 1899, stated,

"Epilepsy is a rare complication of pregnancy and as a rule does not influence unfavorably the course of gestation. Convulsions are often absent during pregnancy and sometimes do not make their appearance until after the child is weaned." It is interesting to bear this opinion in mind and contrast it with a statement of opinion made in Williams' *Textbook of Obstetrics* in 1903. On the subject of epilepsy Williams concluded, "The disease appears to have no effect upon pregnancy though at the time of labor it may be mistaken for eclampsia by inexperienced observers. If the attacks are frequent the patient should be put upon large doses of potassium bromide and treated just as at other times. As a rule it is not advisable to allow the mother to nurse her child, as lactation sometimes appears to aggravate the disease while serious injury might possibly be done to the child during an attack. On the other hand, in occasional instances the mentality of the patient appears to undergo progressive deterioration with each succeeding pregnancy. In such circumstances pregnancy should not be interrupted but the advisability of sterilization after delivery should be considered."

Sachs of Germany in 1910 published his opinion to the effect that pregnancy has no predictable influence one way or another on epilepsy. He dogmatically stated, however, that status epilepticus when it occurs during pregnancy is always fatal to both mother and child. About ten years ago there was considerable material to be found in the German literature on the relationship between epilepsy and eclampsia. Poten in 1925 wrote on this subject and concluded that both were really one and the same disease while Zangemeister partially shared this view and in 1926 went on record as believing that 2 per cent of eclamptics are left suffering from epilepsy as a residual.

Waldstein's interest in this question was keenly stimulated by a case of his own at the Womans Hospital in Vienna. He published this case report in 1928 together with a review of the French and German literature to date on the case reports of 23 epileptics. These 24 women had 54 pregnancies, 40 of which ended spontaneously at term, 4 prematurely, and 10 as early abortions. Waldstein concluded from this study that 50 per cent of epileptics are improved during pregnancy. He held to the belief that epilepsy and eclampsia are separate and distinct diseases.

In Australia, in 1927, at a meeting of the Victorian Branch of the British Medical Association, A. E. Fraser presented a case which stimulated some interesting discussion relevant to the problem of pregnancy in the epileptic patient. The consensus regarding the question of the transmissibility of epilepsy was that heredity was not so pronounced a factor as was generally supposed.

In 1928 in the *Journal of the American Medical Association,* Williams published an article entitled "Indications for Therapeutic Sterilization in Obstetrics." This was a summary of the indications for sterilizations that had been done in his clinic up to the time of publication of the article. There were three patients sterilized because of epilepsy, and when discussing this indication he stated, "Each year a number of epileptic women pass through our hands and we have gained the impression that, in general, epilepsy has no effect on pregnancy or vice versa. Nevertheless, we have sterilized 3 patients sent to us by the psychiatrists with the statements that one had suicidal tendencies and that all showed signs of mental deterioration and that it was probable that the continuation of pregnancies would hasten the process." At the present time so far as I can gather from conferences with the psychiatrists of the same clinic that referred the above mentioned patients to Williams they are not by any means convinced that pregnancy has any predictable influence on epilepsy.

In 1931 Struthers of London reported three cases of epilepsy which had their onset associated with pregnancy and none of these patients had a family history of epilepsy or any suggestive personal past history, and in 1934 Hayden reported his case of a known epileptic who had a convulsion during the second stage of labor. The child was born alive and in good condition. In the *Practitioners Library of Medicine and Surgery,* published in 1936, Greenhill states, "Epilepsy usually has no effect on pregnancy or labor but it may be mistaken for eclamptic convulsions. Treatment is the same as in the nonpregnant state. Nursing should be forbidden

because sometimes this aggravates the attacks. Furthermore, if the mother were to have an attack while the baby were nursing at the breast the child might be seriously hurt. In some cases pregnancy aggravates epilepsy and in these instances further conception should be prevented by contraception or by a sterilization operation.'' Here again it is interesting to note a general statement of opinion and a hurried statement concerning the exceptions. And again, another textbook rather dogmatically stating the deleterious consequences of the effect of nursing on the course of the disease. One suspects that these dogmas may be perhaps begged, borrowed, or stolen from one text to another.

The question of the hereditary factor in epilepsy has undergone some drastic changes of outlook in recent years with such men as William Lenox of Boston and others compiling critical statistics on the incidence of epileptic heredity. Although there still remains much work to be done in this field the recent studies point to the conclusion that the incidence is not nearly so great as it was assumed to be not very long ago. In the most recent edition of the *Oxford System of Medicine,* Lenox very convincingly reports an exhaustive and thorough statistical study which reveals an heredity incidence of about 10 per cent, and he concludes that this may be a generous figure.

In this connection one other point comes to mind. How much is the mild epileptic patient with normal mentality influenced by the superstition, mystery and stigmas associated with this affliction in the minds of most laymen? Who knows but that this influence itself may contribute somewhat to the mental changes which are observed in many epileptics as they go through life, looked upon by many of their fellow men as being ''possessed of a demon.'' Dostoievsky, the famous Russian literary genius, himself an epileptic, paints a vivid picture in his book *The Idiot* of an epileptic during a seizure and also points out the unfavorable and unhealthful light in which the epileptic himself realizes he is being viewed by society. Unfortunately, until very recently students of this disease drew their conclusions from studies of institutionalized patients, which group is by far the minority of epileptics. Bridge, in 1930, with this point in mind showed that studies including noninstitutionalized private patients reveal a less foreboding outlook.

From the reports obtained from the literature to date it is obvious that the relationship between epilepsy and pregnancy has not engaged the attention of physicians to any great extent. It seems appropriate, therefore, at this time to study a series of case histories in the hope of shedding some light on the problem and this was attempted by making a survey of the case records from the three largest maternity clinics in Baltimore, namely, The Baltimore City Hospital, The University of Maryland Hospital and The Johns Hopkins Hospital.

Epilepsy has not been indexed in the records of these three hospitals during certain years and some case records, particularly the early ones, leave much to be desired. Nevertheless, records were found of 37 patients treated in the obstetrical clinics of these institutions which were diagnosed as pregnancy complicated by idiopathic epilepsy. The cases have been studied particularly from the standpoint of the effect of pregnancy on the epilepsy and with the exception of 3, the cases seemed to

fall into one of 4 separate groups; those in which there was no effect; those made worse; those which were improved and a fourth group in which the onset of the epilepsy was associated with pregnancy. The more interesting facts are set down in Table I, and a few individual cases are recorded as representative of each group.

TABLE I. CLASSIFICATION

	NUMBER OF CASES	NUMBER OF PRIMIPARAS	NUMBER OF MULTIPARAS	AVERAGE AGE YEARS	AVERAGE AGE ONSET OF EPILEPSY YEARS	EPILEPSY RELATED TO MENSES	AVERAGE FREQUENCY OF ATTACKS	
							NON-PREGNANT	PREGNANT
No change	21	10	11	25	14	3	Every two weeks	Every two weeks
Improved	5	5	0	20.6	14.2	4	Monthly	Every six months
Worse	4	2	2	23.2	12.3	0	Every six weeks	Every two weeks
Began with pregnancy	4	2	2	19.5	19.5	–	0	Every two months
Unclassifiable	3	1	2	25.6	?	?	–	–

The most conspicuous fact revealed in the study is that a considerable majority (21), of the cases fell into the group in which the pregnancy had no effect on the epilepsy. There were 10 primiparas and 11 multiparas in this group and the average frequency of the attacks was every two weeks. Conversely, in no case in the entire series did the epilepsy have any effect on the pregnancy except in those cases in which the disease was misinterpreted as eclampsia and delivery was unnecessarily radical. This mistake was made in 5 of the 37 cases in the series and the patients treated as eclamptics. The following case illustrates that group in which the epilepsy was not influenced by the pregnancies and also brings out the possibility of a wrong diagnosis:

A. R., white, with a negative epileptic family history, began to have convulsions at the age of 15 years. The attacks appeared irregularly but averaged one seizure every two to three weeks. At the age of 20 she became pregnant and throughout gestation there was no change in the frequency of the attacks. One week before term a convulsion occurred, and she was hospitalized. Although the blood pressure was normal and the urine contained only a trace of albumin, a diagnosis of eclampsia was made and labor was induced with a Vorhees' bag. After a four-hour labor she spontaneously delivered a full-term, living normal child. The history of previous fits was not obtained until after labor was induced. She was put on luminal therapy and did not suckle the child and the puerperium was uncomplicated except for a typical epileptic seizure on the fifth day. On continuous luminal and bromide therapy, the attacks continued every two or three weeks. At the age of 22 years she became pregnant again and was delivered spontaneously at term of a living child in the same clinic. The frequency of the attacks still remained unchanged when she was seen at a one-year follow-up, not pregnant. Both children were apparently normal at that time.

Five of the patients in the study were definitely improved during their first pregnancy. Unfortunately none of these patients were seen again

during a subsequent gestation if any occurred. The average frequency of attacks before gestation was once monthly and during the pregnancies the average frequency was once every six months. This improvement cannot be accounted for by the institution of sedative therapy because in only one of these cases was this done early in gestation, and in that case the frequency of the attacks after delivery was approximately the same as before conception. One fact, however, seems significant in the histories of this group; in 4 of these there was a definite relation between the epileptic seizure and menstruation. The association of epilepsy with menstruation is a matter of common medical knowledge, and because of the intimacy of menstruation and reproduction, an attempt was made to determine from each history in this survey whether or not the patient's attacks were associated with the menses. In 7 of the cases there was a definite relationship and 4 of these fell into the improved group and 3 in the group which revealed no change. One suspects that a larger series may reveal a definite tendency toward improvement during pregnancy in this type of case, which might well have a logical physiologic rationale. This group is well illustrated by the following case:

G. B., colored, with a generally contracted rachitic pelvis and a negative epileptic family history, began to have typical epileptic fits at 13 years of age, once each month close to the menstrual period. At the age of 19 she became pregnant and during gestation she had only 3 seizures, one each in the second, fifth, and sixth months. She was delivered at term of a normal living child by elective cesarean section because of cephalopelvic disproportion. On the sixth post-partum day she had 3 epileptic convulsions (the child was not breast fed). Following this episode she was put on daily luminal therapy and she had one convulsion two months post partum when her menses appeared. Four months after delivery she again became pregnant and had no attacks throughout the gestation. She was again delivered of a normal child at term by cesarean section and sterilized by tubal ligation, and the puerperium was free from attacks. Although she was instructed to return for a follow-up, she was never heard from again.

Four patients fell into the group which were made worse by pregnancy. Two were primiparas and 2 were multiparas whose average frequency of attacks in the nonpregnant state was every six weeks and during pregnancy was every two weeks. In none of these cases was there any relation between the attacks and menstruation. The following case is representative of this group:

M. T., white, whose mother gave a history of grand mal attacks which occurred at irregular intervals since the puerperium of her first pregnancy. There was no change in the frequency of the mother's attacks throughout 3 subsequent pregnancies. The patient gave a history of petit mal attacks "all her life," described as fleeting attacks of fainting preceded by feelings of unreality, occurring irregularly. At the age of 24 she had two typical grand mal attacks within one week, and subsequently the petit mal attacks occurred as before until the age of 26 when she became pregnant. During the first six months of gestation she had 8 grand mal attacks spaced at fairly regular intervals. She was put on daily luminal, and during the last four months of pregnancy had 3 major seizures. At term she was delivered spontaneously of a living normal child and the puerperium was uncomplicated except for a major epileptic fit on the third, fifth, and twelfth days (child not breast fed). During the following eighteen months she had 4 major seizures but no petit mal attacks, and then became pregnant again. During this second gestation a

major epileptic attack occurred about every three weeks on luminal therapy. She delivered a full-term child spontaneously and the puerperium was free from attacks. She was followed no further.

The fourth classifiable group comprises those patients whose initial attack of epilepsy was associated with pregnancy. There were 2 primiparas and 2 multiparas; in none of this group was there a family history of epilepsy and nothing suggesting petit mal in their personal past history. In 3 of the cases the seizures began during the first pregnancy and occurred at irregular intervals thereafter. In the other case the fits occurred in the puerperium of the second pregnancy and is here recorded to illustrate this group:

R. V., colored, with negative past history was delivered spontaneously at term at the age of 16. Again at term she was delivered spontaneously at the age of 17 and two days postpartum had a typical epileptic convulsion (the child was breast fed). The attacks occurred irregularly during the next seven years and in this interval she had 5 normal term children and there was no change in the epilepsy throughout these gestations. During her eighth pregnancy the attacks disappeared entirely and remained absent for the following six months, when at the age of 26 she became pregnant for the ninth time. During the first twelve weeks of this pregnancy she had 26 convulsions at approximately regular intervals. During this episode sedative therapy gave no relief and therapeutic abortion and sterilization were done. At a six-week follow-up she reported 3 convulsions since the abortion. She was not heard from again.

Three cases in this study were placed in an unclassifiable group because these patients were idiots with arrested mentality, and it was impossible to gain any information from the histories. However these patients delivered infants that were apparently normal.

Aside from the information given in the table the following facts were revealed by this study: The years in which epilepsy was indexed in the hospitals surveyed represent a total of 54,688 patients treated, an incidence of 0.067 per cent. The fetal and maternal mortality was zero, and so far as they were followed, the babies were apparently normal.

The clinical characteristics of the convulsion, per se, will not serve to differentiate eclampsia from epilepsy. It must also be remembered that the blood pressure may be temporarily elevated during an epileptic seizure and the convulsion is frequently followed by a moderate albuminuria. The postconvulsive coma of eclampsia usually appears deeper and more prolonged than that following an epileptic attack and the hypertension more persistent. The presence of edema with marked hypertension and urinary changes point toward eclampsia but the most valuable differential point, however, is the history of epilepsy, writ large. In some cases even this will not hold as the present study reveals that the number of cases in which the initial epileptic attack is associated with pregnancy is slightly higher than would seem to be coincidental. In a recent survey of eclampsia over a five-year period in the entire state of Maryland, Reese and Peyton found an incidence of 0.2 per cent or one case of eclampsia in every 500 deliveries, while in the survey included in this paper the incidence of epilepsy complicating pregnancy is 0.067 per cent or one case in every 1,500 deliveries. Eclampsia, then, occurs three times as often as epilepsy in pregnant women, so that, in

the differential diagnosis of eclampsia and epilepsy alone, excluding the possibility of convulsions of other etiology, one in every four pregnant women having convulsions should be an epileptic. We should refrain, therefore, from jumping to conclusions too readily when we see a pregnant patient in a convulsive seizure. Treatment by sedation is, of course, of value in either condition but the prognosis is alarmingly different.

CONCLUSIONS

From the reports and opinions available and the facts revealed in this study, it appears that the following attitude may justifiably be taken by the obstetrician:

Epilepsy has no appreciable effect on the course or termination of a pregnancy.

The reports of the effect of pregnancy on epilepsy are both conflicting and confusing. The investigation of 37 case histories indicates that there is no general rule by which we can be guided, although in the majority, pregnancy has no effect on the epilepsy. Therefore, like so many other problems in obstetrics, the treatment and disposition of the pregnant epileptic will depend upon the merits of each individual case, and it seems that the number of patients who will require special handling will be in the minority.

In the light of recent clearer knowledge the obstetrician may be of infinite help to his pregnant epileptic patient; first, by dispelling the mysterious superstition which surrounds the disease he may establish a more helpful, less pessimistic attitude of mind regarding her own outlook. Next, he should assure her that the probability of the transmission of the disease to her offspring is not so great as she probably thinks it is.

One final conclusion seems more certain. By specifically inquiring about the occurrence of seizures suggesting petit mal or grand mal at the first prenatal visit we may spare ourselves a subsequent "pseudo-eclamptic" surprise.

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UTERINE MOTILITY RESULTING FROM INFLAMMATORY PROCESSES IN THE MYOMETRIUM, IN THE ABSENCE OF OVARIAN HORMONES*

MAURICE W. LAUFER, M.A., AND SAMUEL R. M. REYNOLDS, PH.D.,
BROOKLYN, N. Y.

(From the Department of Physiology, Long Island College of Medicine)

AT THE present time it is generally held that one may induce motility of uterine muscle in ovariectomized rabbits in only one way,[3, 5] namely, by the injection of ovarian follicular hormone or other estrogenic agents. When it was found, however, that suitable degrees of chronic distention of the uterus elicit hypertrophy[6] and hyperplasia[1] of the myometrium of ovariectomized rabbits it seemed likely that one would find motility associated with these structural changes. Although distention did not induce motility, it was found that, in certain experiments in which inflammatory processes were present, uterine motility was induced. The procedures were as follows:

Six mature, isolated rabbits were injected with prolan in order to bring all the animals into a comparable state of pseudopregnancy. On the seventh day, the ovaries were removed and one week later, uterine fistulae were prepared in the usual manner.[3] At this time, a ligature was passed about the tubal end of the left uterus in each case. On the third day following this operation, the left uterine cornu was distended with physiologic saline (2 or 4 c.c.) without aseptic precautions. In order that the saline would be retained, a purse-string suture was passed about the orifice of the uterus which was exposed in the preparation of the fistula. The fluid was allowed to remain in place until the fourth day later; at this time the growth-effects of chronic distention are about complete.[7]

As a result of these procedures, six rabbits were available at the end of the third week after ovariectomy, each one of which possessed one uterine cornu (left) developed in response to chronic distention and another uterine cornu (right) which was undistended and undergoing atrophy of castration (Fig. 1). Such atrophying uteri are invariably nonmotile and are unreactive to the usual oxytocic agents, except epinephrine.[8]

The spontaneous motility of both uterine cornua in each rabbit was simultaneously recorded from the unanesthetized rabbits on the fourth day after distention and the reactivity to pilocarpine and epinephrine determined. Pilocarpine was used, since in the experience of one of us it is effective only on uteri that are motile under the influence of

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estrin.[4, 8] After recording these motility responses, the rabbits were sacrificed and each uterine horn dissected free and weighed. The amount of enlargement taking place in each instance was determined by comparing the weight of the distended horn (empty) with the corresponding undistended horn from the same rabbit. Sections from each uterus were also taken for histologic study. Under the foregoing conditions the following results have been obtained:

Spontaneous Motility.—Three of the distended uteri were highly active, showing a succession of major contractions of varying durations and frequencies. Although the uteri were highly active, the motility was characterized by great irregularity (arrhythmicity), as shown by the examples in Fig. 2. This motility stands in marked contrast to the regular or rhythmic type of uterine motility which follows the administration of estrin (Fig. 3). The undistended or control uterine fistulae showed no measurable motility (cf. Rabbit 4, Fig. 2), although the

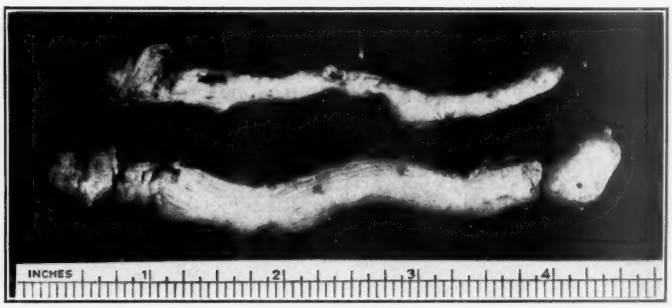

Fig. 1.—Uterine cornua from Rabbit 4. Dissected free and fixed in formol-acetic fixative. Top, undistended cornu; bottom, emptied cornu after four days of chronic distention with fluid. Weights, 3.27 gm. and 9.11 gm., respectively. See Fig. 2 for motility records.

balloons in the two uteri were of the same size and under the same distending pressure (20 cm. of water).

The experimental horns in the remaining three rabbits were almost completely inactive; they showed very feeble, irregular activity which was little different from that seen in the control horns. The latter were quiescent, as is normally the case this length of time after ovariectomy.[3] Consequently, no uterine motility was induced in these three rabbits by the distention method employed in these experiments. The amount of uterine enlargement which took place is described below. Suffice it to say now that motility was induced in only three of the six rabbits although appreciable uterine enlargement occurred in the distended uteri of all the rabbits. Clearly, therefore, the motility observed in these experiments depends upon some factor other than uterine growth resulting from the stimulus of distention; this factor was found to be local inflammatory processes, as noted below.

Reactivity to Pilocarpine.—Five to 6 mg. of pilocarpine-HCl were injected intravenously once or twice in each rabbit. The usual elevation of tone which one sees in estrin-treated rabbits receiving pilocarpine was lacking in every instance in the present experiments, even in those uteri showing considerable activity. A characteristic uterine response to pilocarpine in an estrin-treated rabbit is shown in Fig. 3, and the absence of such an effect in the present experiments is shown in the

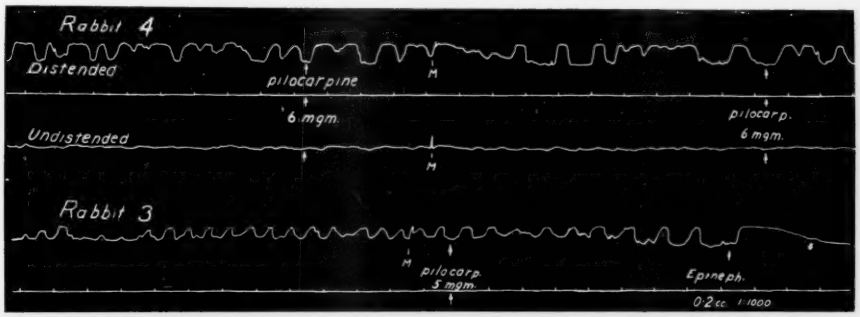

Fig. 2.—Uterine motility in untreated, ovariectomized rabbits (unanesthetized) whose uteri were distended for four days with fluid. Motility was observed when there were inflammatory conditions in the myometrium but not otherwise, even though growth resulted from the distention. Note lack of regularity of contractions and lack of uterine response to pilocarpine. Time, minutes.

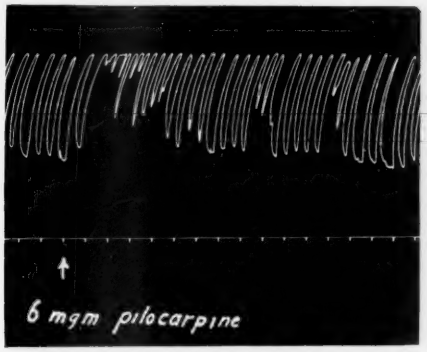

Fig. 3.—Uterine motility in estrin-treated rabbit, unanesthetized. Note the regularity of the contractions and the response to pilocarpine lasting for more than four minutes.

records of Fig. 2. The pilocarpine was effective otherwise in these rabbits, however, since excessive salivary and lachrymal gland stimulation occurred and a large amount of fecal material was passed after each injection.

In summary, it may be said that the motility which was induced by inflammation in these uteri differed in two respects from that which follows the injection of estrin in ovariectomized rabbits. First, it lacked coordination and rhythmicity characteristic of the estrin response, and second, the distention-activated uteri were unresponsive to pilocarpine

in contrast to the responsiveness to this drug of the estrin-activated uterus. Typical epinephrine responses were regularly obtained, however, indicating the recording capability of the technical procedures in each case.

Motility in Relation to Growth and Histologic Changes.—The percentage increases in size of the distended uteri over the nondistended uteri ranged from 18 per cent at one extreme to about 189 per cent at the other. Marked motility was observed in uterine cornua showing 18 per cent, 178.6 per cent, and 189.2 per cent increases in size. The relatively nonmotile or feebly active experimental uteri showed percentage increases of 75.6 per cent, 106.4 per cent, and 108.3 per cent, respectively. Consideration of these results will show that the motility which was induced by distention is not dependent upon growth changes taking place, since the uterus showing least growth was highly active and, conversely, appreciable enlargement occurred in the three nonmotile uteri. Examination of the histologic changes which are associated with the occurrence of motility in these experiments has proved fruitful, however.

The control or undistended uteri in all cases presented a picture of castration atrophy such as has been described.[6] The cells were small, the cytoplasm densely staining; the glands were inactive and the tissues relatively avascular. The experimental uteri presented a contrasting picture: the cells were large, the nuclei vesicular, the cytoplasm increased in amount, the tissues more or less edematous, and the epithelium of the endometrium was tall columnar in type and actively secreting. The growth responses were particularly prominent in the myometrium of all the experimental uteri. Inasmuch as three of these were quiescent, however, it is clear that growth resulting from chronic distention is not, per se, a stimulus for myometrial activity. The nonmotile uteri were free of inflammation, except in the most superficial portion of the endometrium. In striking contrast to this observation is the fact that inflammatory changes were a conspicuous feature in each of the active uteri, being especially prominent in the vascular zone of the myometrium. Here, marked hyperemia was observed and prominently associated with this in each case was the infiltration of large numbers of polymorphonuclear cells throughout the tissues. Although these cells were most numerous in the superficial portions of the endometrium they were also present in considerable numbers in the tissues about the vascular zone in the myometrium. In the inactive experimental uteri this inflammatory condition of the myometrium was conspicuously absent.

DISCUSSION AND SUMMARY

When the uterine fistula of an untreated, ovariectomized rabbit was distended with fluid for four days, growth of all the tissue components took place. ***In the absence*** of irritative changes in the myometrium, no

uterine motility was observed. Accordingly, neither chronic distention and the associated anabolic changes which resulted therefrom, nor the balloon, the presence of which constituted a "foreign body" within the uterus when the motility was being studied, were motility-provoking agents. In the cases in which motility was observed, histologic evidence of inflammation in the myometrium was present. This consisted of marked hyperemia of the vascular zone, edema of the tissues, and infiltration of the uterine tissues with polymorphonuclear cells.

It was found that the features of the motility obtained under the conditions of these experiments differed in two ways from that which results from the administration of estrin to ovariectomized rabbits. In the first place, the motility which is associated with inflammation of the myometrium in these experiments is arrhythmic, whereas that which follows the injection of estrin is rhythmic. In the second place, uteri which were motile because of an associated inflammatory condition of the myometrium were found to be unreactive to pilocarpine administration in amounts which were highly effective in estrin-activated uteri. The nature of these differences between the two types of motility remains to be elucidated.

It may be pointed out in conclusion, however, that both types of motility have one feature in common. The uterine motility which results from the action of estrin is preceded by marked hyperemia and edema of the uterine tissues,[2, 5] and in the present experiments motility is observed when marked hyperemia and edema of the vascular zone in the myometrium occur. Investigation of the rôle of hyperemia in the initiation of uterine motility should prove fruitful.

We are indebted to Howard R. Gerber for technical assistance in these experiments.

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In 1923 Mondor and Huet reported only 38 known cases of mucous cysts of the labia minora. The author adds an observation of his own. The author feels with Schauta and Kollmann that although wolffian body rests have not been demonstrated in this area, it is possible that there might be an alteration of wolffian epithelium in this area to form a mucous cyst.

MARIO A. CASTALLO.

ANALGESIA DURING THE FIRST STAGE OF LABOR

Further Study of Dilaudid-Scopolamine

Walter A. Ruch, M.D., Memphis, Tenn.

(From the Department of Obstetrics, University of Tennessee, College of Medicine)

OF THE 755 cases in this series, I[1] reported 101 cases, taken in part from private practice and in part from the obstetric service of the University of Tennessee Medical School, in May, 1934. The remaining 654 cases are all from private practice.

Our previous study was essentially a comparison of dilaudid-scopolomine and morphine-scopolamine as to speed of action, quality of analgesia in the mother and depressive symptoms in the baby. Our results were so definitely in favor of dilaudid-scopolamine that we continued to use it in all of our cases. In view of our further experience with this combination, an analysis of all our results with it seems desirable at this time. In the present series, dilaudid in combination with scopolamine was used exclusively for first stage seminarcosis and various types of anesthesia (ethylene, nitrous oxide, ether) were used for the second stage. In part of the series, nembutal and sodium amytal were used in 3 and 6 gr. doses, respectively. In some cases where the patients were extremely nervous and apprehensive, these barbiturates were given early, preceding the use of the dilaudid combination, and in others it was given later, where the patient had become restless, for a greater degree of narcosis.

The results of the combined series have been outlined in tabular form to show the time elapsing between the original dose of the drugs and the breathing of the baby, the quality of narcosis obtained in the mother, and the effect of the drug upon the baby. No attempt has been made to indicate the para nor to outline the number of doses given of either drug, nor the exact dosage in each individual case.

By the term "slight asphyxia" as used in the tables we mean simply a slight delay of twenty to forty seconds in the cry or breathing of the baby. Perhaps the word "apnea" as used by Eastman[2] is a better term for this condition. All of these babies began to breathe after removing mucus from the throat or following minor resuscitative measures, such as gentle rubbing of the back or thumping of the feet. The term "deep asphyxia" as used in the tables was applied to babies who showed prolonged asphyxia and included the stillborn babies as well as those who had asphyxia livida or asphyxia pallida.

In the 270 cases of this group, all had dilaudid-scopolamine during the first stage and ethylene-oxygen for the second and third stages. Good analgesia was obtained in 235 of the cases; the remaining 35 obtained only fair analgesia. In 254 of the babies (94.1 per cent) crying and respiration were spontaneous. Slight asphyxia was present in 15 babies (5.6 per cent). There was one stillborn baby who had asphyxia pallida due to an intracranial hemorrhage resulting from a rapid second stage in a multipara.

TABLE I. FIRST STAGE DILAUDID-SCOPOLAMINE. SECOND STAGE ETHYLENE-OXYGEN

TIME BETWEEN FIRST DOSE AND DELIVERY	NUMBER OF CASES	EFFECT OF ANALGESIA		CONDITION OF BABY		
		GOOD	FAIR	SPONTANEOUS CRY	SLIGHT ASPHYXIA	DEEP ASPHYXIA
Less than one hour	0					
One to two hours	45	15	30	45	0	0
Two to three hours	0					
Three to four hours	45	45	0	35	10	
Four to five hours	60	60	0	59	0	1 Stillborn
Five to six hours	70	67	3	66	4	
Six to seven hours	50	48	2	49	1	
Seven to eight hours	0					
Eight to nine hours	0					
Nine hours and over	0					
Total	270	235	35	254	15	1

In this series of 75 cases nembutal (1½ gr.) and sodium amytal (3 gr.) were given interchangeably prior to the administration of dilaudid-scopolamine. The resulting analgesia was good in all cases and only 3 babies (4 per cent) exhibited slight asphyxia and none had deep asphyxia.

TABLE II. FIRST STAGE BARBITURATE AND DILAUDID-SCOPOLAMINE. SECOND STAGE ETHYLENE-OXYGEN

TIME BETWEEN FIRST DOSE AND DELIVERY	NUMBER OF CASES	EFFECT OF ANALGESIA		CONDITION OF BABY		
		GOOD	FAIR	SPONTANEOUS CRY	SLIGHT ASPHYXIA	DEEP ASPHYXIA
Less than one hour	0					
One to two hours	0					
Two to three hours	0					
Three to four hours	30	30	0	29	1	
Four to five hours	20	20	0	20	0	
Five to six hours	22	22	0	21	1	
Six to seven hours	3	3	0	2	1	
Seven to eight hours	0					
Eight to nine hours	0					
Nine hours and over	0					
Total	75	75	0	72	3	

All of the 219 cases summarized in Table III had dilaudid-scopolamine in the first stage and nitrous oxide-oxygen in the second and third stages. The general analgesic effect in this group was good and only 6 babies (2.7 per cent) showed slight asphyxia. Two babies were stillborn as a result of a prolonged period of "molding" in primiparae followed by asphyxia pallida.

TABLE III. FIRST STAGE DILAUDID-SCOPOLAMINE. SECOND STAGE NO_2O_2

TIME BETWEEN FIRST DOSE AND DELIVERY	NUMBER OF CASES	EFFECT OF ANALGESIA		CONDITION OF BABY		
		GOOD	FAIR	SPONTANEOUS CRY	SLIGHT ASPHYXIA	DEEP ASPHYXIA
Less than one hour	12	3	9	12	0	
One to two hours	16	16	0	15	1	
Two to three hours	34	34	0	33	1	
Three to four hours	36	36	0	36	0	
Four to five hours	50	49	1	48	2	
Five to six hours	19	19	0	19	0	
Six to seven hours	13	13	0	12	1	
Seven to eight hours	10	10	0	10	0	
Eight to nine hours	14	14	0	13	1	
Nine hours and over	15	14	1	13	0	2 Stillborn
Total	219	208	11	211	6	2

In this group of 58 cases, nembutal (3 gr.) and sodium amytal (6 gr.) were given late in labor for restlessness and 7 babies (12 per cent) showed slight asphyxia, and there were none with deep asphyxia.

TABLE IV. FIRST STAGE BARBITURATE AND DILAUDID-SCOPOLAMINE. SECOND STAGE NO_2O_2

TIME BETWEEN FIRST DOSE AND DELIVERY	NUMBER OF CASES	EFFECT OF ANALGESIA		CONDITION OF BABY		
		GOOD	FAIR	SPONTANEOUS CRY	SLIGHT ASPHYXIA	DEEP ASPHYXIA
Less than one hour	2	2	0	2	0	
One to two hours	2	2	0	1	1	
Two to three hours	4	4	0	2	2	
Three to four hours	8	8	0	7	1	
Four to five hours	4	4	0	4	0	
Five to six hours	4	4	0	3	1	
Six to seven hours	6	6	0	6	0	
Seven to eight hours	4	4	0	4	0	
Eight to nine hours	2	2	0	2	0	
Nine hours and over	22	22	0	20	2	
Total	58	58	0	51	7	

The patients of this group received ether anesthesia in the second and third stages following dilaudid-scopolamine first stage analgesia. There were only 18 in this group, and out of this number 11 (61 per cent) showed slight asphyxia livida and 3 breathed normally only after several minutes of resuscitation and the administration of carbon dioxide-oxygen. It is interesting to compare the ether group with those receiving other anesthetics for the second and third stages. In the 737 patients receiving ethylene or nitrous oxide, a delay in cry or breathing, in no case lasting over forty seconds, occurred in 31 cases (4.2 per cent). Only where ether was used was there any marked asphyxia and there is no doubt in our minds that it was the offending factor.

Since smaller doses of dilaudid as well as of scopolamine had been reported,[3-5] for obstetric or surgical analgesia, we varied the size of the dose of both drugs in a number of cases. A combination of $\frac{1}{32}$

TABLE V. FIRST STAGE DILAUDID-SCOPOLAMINE. SECOND STAGE ETHER

TIME BETWEEN FIRST DOSE AND DELIVERY	NUMBER OF CASES	EFFECT OF ANALGESIA		CONDITION OF BABY		
		GOOD	FAIR	SPONTANEOUS CRY	SLIGHT ASPHYXIA	DEEP ASPHYXIA
Less than one hour	0					
One to two hours	0					
Two to three hours	6	6	0		4	2
Three to four hours	2	2	0		2	
Four to five hours	0					
Five to six hours	0					
Six to seven hours	2	2	0		1	1
Seven to eight hours	2	2	0		2	
Eight to nine hours	0					
Nine hours and over	6	6	0	4	2	
Total	18	18	0	4	11	3

gr. of dilaudid and $\frac{1}{130}$ or $\frac{1}{200}$ gr. of scopolamine was used (Burroughs-Wellcome hyoscine hydrobromide was used throughout the series). Likewise dilaudid $\frac{1}{48}$ gr. was used with $\frac{1}{130}$ or $\frac{1}{200}$ gr. of scopolamine. We were unable to see any advantage in the smaller doses of either dilaudid or scopolamine, and since no ill effects were noted in this study, we are satisfied that for a patient of average weight the dosage used in the technique outlined in our previous report is the proper one. This method is as follows: $\frac{1}{32}$ gr. of dilaudid and $\frac{1}{130}$ gr. of scopolamine are administered subcutaneously when the cervix is dilated $3\frac{1}{2}$ to 4 cm. in primiparae and $2\frac{1}{2}$ cm. in multiparae; forty-five minutes later, $\frac{1}{130}$ gr. of scopolamine; forty-five minutes later, a dose of $\frac{1}{260}$ gr. of scopolamine, repeated again in forty-five minutes, and thereafter every one or two hours. There can be no set routine for seminarcosis. As Weum stated, every parturient woman needs individual care, and it is impossible to give any definite routine to be followed in all cases. After studying a large series of cases, it is almost possible to forecast the type of narcosis obtained in a particular type of patient, even before the drug is administered.

Several other interesting observations were made while studying this series of cases. For example, in a few cases (primiparae) delivery was made by forceps and episiotomy without anesthetics because of a decompensated heart, and there were absolutely no ill effects from the administration of dilaudid-scopolamine.

Another interesting observation was made on some of the babies. Several were x-rayed on the second day of life for the purpose of determining whether or not they had an enlarged thymus gland. Some of these babies were from mothers who entered the hospital too late for seminarcosis, others were included in the series. From a study of the x-ray plates in 378 cases, it was found that in 24 babies atelectasis was present although but one of these babies showed active

symptoms. In all but 4 or 5 babies the lungs were completely expanded at the end of three to five days. The only baby who showed definite symptoms of atelectasis clinically failed to clear up within the few days' period, but was all right at the end of one month. Several babies who showed slight atelectasis in the x-ray pictures were from mothers who had no seminarcosis during the first stage.

SUMMARY

In a series of 755 cases, $\frac{1}{32}$ gr. of dilaudid and $\frac{1}{130}$ gr. of scopolamine proved to be a satisfactory combination for the production of seminarcosis during the first stage of labor, providing a pleasing analgesia for the mother with little, if any, effect on the baby. In some cases a small dose of one of the barbiturates was administered in conjunction with dilaudid-scopolamine analgesia. When ethylene or nitrous oxide was used for anesthesia in the second and third stages, apnea occurred in only 4.2 per cent of the babies. With ether, respiratory difficulty was encountered more frequently.

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EXPERIMENTAL TRANSPLANTATION OF THE OVARIES

Autotransplants of Dog Ovary Into Omentum

George H. Romberg, M.D., White Plains, N. Y.

(From the Gynecological Service and the Laboratories of Mt. Sinai Hospital, New York)

SINCE the publication of the preliminary report by the author,[1] in which a brief summary of the literature was listed, there has continued widespread and increasing interest in the subject of ovarian transplantation. The recent literature adds little that is really new, but serves to crystallize the knowledge of the subject. An excellent review of the subject can be found in the Report of the French Surgical Association (XLV Surgical Congress), published in 1936.[2]

In this communication we report further experimental studies done with autotransplants of dog ovary into the omentum. In the preliminary report we presented the histologic findings of autotransplants and homotransplants which had been removed for study after three months.

It is generally known that functional transplanted tissue of a few weeks' duration may at a later date present an entirely different picture with disappearance of most, if not all, of the functional elements; that

fibrosis, cellular infiltration and degeneration may ensue. It was with this thought in mind that this second series of experiments was carried out. The transplants in this series were observed at the end of eight and nine months. Only autotransplants were used in this second series.

In the previous experiments done by the author, the ovary was simply bisected and then sutured to the omentum after enveloping the omentum about the transplant. In the experiments reported here varying-sized portions of ovary and a varying number of fixation sutures were used to determine the effect on the final appearance of the graft. A discussion on this point will be given below.

EXPERIMENT I

The right ovary of a dog was removed under aseptic conditions, and bisected. One half of the ovary was sutured to the adjoining margin of the omentum in

Fig. 1.—Photomicrograph of large implant showing follicles in all stages of development. Portion of corpus luteum in corner. Ovarian transplant eight months old.

such a manner that it was completely enveloped by the omentum. Long black silk sutures were used for future identification. The remaining portion of the ovary was divided into halves and one of these was again divided into equal parts. These fragments were similarly sutured to the omentum.

Transplants were removed approximately eight months later.

The histologic sections (hematoxylin-eosin stain) show functioning ovarian tissue. The photomicrograph of the larger transplants (Fig. 1) shows many Graafian follicles in all stages of development. There are also numerous primordial and atretic follicles. In this photomicrograph, there can also be seen a portion of a corpus luteum. The detail of the Graafian follicle, including the theca externa and interna, shows up clearly. The section shows only an occasional lymphocyte.

The section of the other transplants shows similar findings, i.e., functioning ovarian tissue with follicles in all stages of development, but these become less pronounced proportionately to the size of the implant. In the smallest implants, measuring approximately 0.5 cm. in diameter, the follicles were chiefly of the atretic variety with only an occasional, moderately-developed Graafian follicle. The collection of lymphocytes was more numerous and the stroma appeared more con-

densed. This condensation was most pronounced in the region of the sutures. The fibrous tissue reaction was minimal. Proliferation of follicular epithelium was less marked in the smaller implants.

EXPERIMENT II

In this experiment, the left ovary of a dog was used. It was exposed and treated as in Experiment I, but the fragments were all cut small, ranging in size from 1 cm. to 0.25 cm. The number of sutures used to fix the ovarian fragments to the omentum varied from one to four. It is needless to add that some difficulty was encountered in handling the smallest fragments.

The histologic findings of these sections show functioning ovarian tissue. They all show follicles in different stages of development with the primordial phases most numerous. The number of large follicles seemed to bear a definite relation to the size of the implant and to the number of sutures used to fix the implant to the omentum. Only in the larger fragments, 0.5 to 1 cm., were Graafian follicles seen. The sections from these fragments show a moderate number of atretic follicles.

Fig. 2.—Photomicrograph of smaller implant showing a Graafian follicle in the center of the field. Atretic follicles most numerous. Adjoining omentum seen. Ovarian transplant eight months old.

In the smallest fragments, 0.25 to 0.5 cm. size, only a few atretic follicles, and some cystlike areas were noted. The fibrous tissue reaction was somewhat more marked than in the larger implants. The stroma was more condensed and the lymphocytic infiltrations seemed more numerous. This infiltration was especially pronounced in the fragments that had more than two sutures. A few giant cells were seen in the area of the sutures. The age of these implants is eight months.

Fig. 2 shows an area from the larger fragment. In the center is a Graafian follicle containing one ovum. The discus proligerus and the theca interna and externa are well defined. There are a few primordial follicles and cystic spaces in the vicinity. The adjoining omental tissue is visible.

EXPERIMENT III

The right ovary of a dog was transplanted as in Experiment I, and removed nine months later. Fig. 3 is a photomicrograph showing a typical area from the largest fragment. There are numerous follicles in all stages of development. The atretic follicles are also well represented. A portion of a corpus luteum is also included in the field. The findings resemble those in Experiment I.

EXPERIMENT IV

The left ovary of a dog was removed and divided into various-sized fragments as in Experiment II. These were attached to the omentum with a number of sutures, varying from 2 to 4. Histologic findings at the end of nine months presented an appearance essentially the same as in Experiment II. In one instance where 4 sutures had been used in a very small fragment, the omentum surrounding

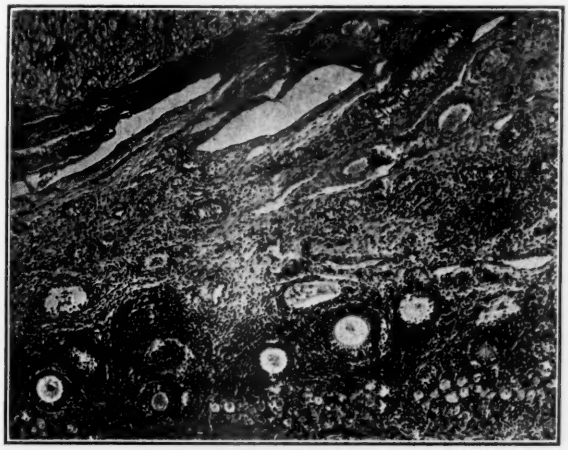

Fig. 3.—Photomicrograph showing an area from a large implant. Ovarian transplant nine months old.

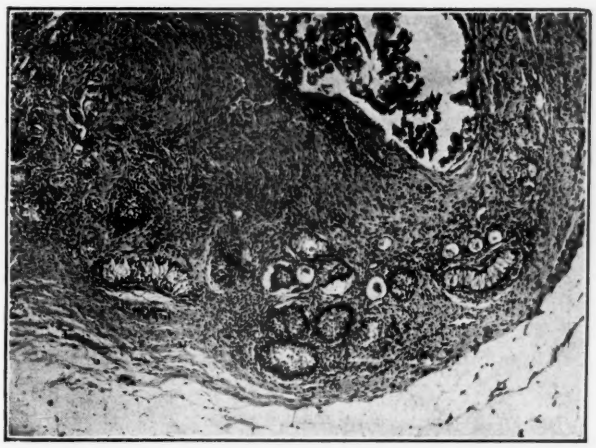

Fig. 4.—Photomicrograph showing an area in a very small fragment that had been heavily sutured. One of the sutures and adjoining omentum shown. Ovarian transplant nine months old.

the implant was found adherent to the lower lateral abdominal wall. The fibrous tissue reaction was quite marked and there was relatively little proliferation of follicular epithelium.

Fig. 4 is a photomicrograph showing an area in a very small fragment that had been heavily sutured. There are a moderate number of developing follicles and a few atretic follicles adjoining the omental fat, except where the suture constricted

the cortical tissue. The lymphocytes are not numerous in this particular section, but were found almost invariably with associated giant cells, especially where the sutures were close to each other.

SUMMARY AND CONCLUSIONS

In the preliminary paper, the results of autotransplants into the omentum were observed up to three months. The ovaries were bisected and only large portions of transplants were used. Definite evidence of functioning tissue was found in all the transplanted ovaries that were examined. The lymphocytic infiltration in the autotransplants was minimal and limited to the area surrounding the silk sutures. This was interpreted as a foreign body reaction, although no giant-cells were seen. The fibrous tissue reaction in the autotransplants was minimal. The proliferation of follicular epithelium was well marked.

In the present series, definite histologic evidence of functioning tissue was found in practically all the sections of the ovaries transplanted. The age of the implants was eight and nine months.

In this series, an attempt was made to learn if the size of the transplant or the number of sutures employed to fix the transplant would alter the final picture. It was noted that the blood vessels in the omentum in the region of the ovarian implant were essentially all of the same size. The blood supply to some of the smallest fragments which showed very little functional tissue seemed well established. (Injection studies of ovarian vessels in the transplants are being carried out, the results of which will be published in a later report.) From the results we could justifiably conclude that the two factors above did make a difference, as evidenced by the lesser number of developed Graafian follicles, the lesser amount of epithelial proliferation in the follicles, and the greater amount of fibrous tissue reaction and lymphocytic infiltration that were found in the smallest fragments, particularly in those which had the more numerous fixation sutures. This could be expressed another way; the more physical handling of the ovarian fragments, the less evidence of functioning ovarian tissue in the transplants.

When we consider the proximity of the omentum to the ovary, its striking powers for rapidly increasing its blood supply and its remarkable reaction to infectious processes, together with the experimental findings described above, we may conclude that the omentum offers an ideal site for autotransplantation of the ovary.

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145 Maple Avenue

THE BLOOD LOSS IN MENORRHAGIA*

ADELAIDE P. BARER, PHD., AND W. M. FOWLER, M.D., IOWA CITY, IOWA
(From the Department of Internal Medicine, State University of Iowa)

IN ORDER to ascertain the amount of blood lost during normal menstruation, determinations were made on 100 women who were not anemic and who considered their menses to be normal in every respect.[1] The results showed a loss of from 6.66 to 178.69 c.c. of blood with an average loss of 50.55 c.c. The hemoglobin loss varied from 0.68 to 23.57 gm. with an average of 5.82 gm. It is impossible to set definite limits of normal, but the average loss for this large a series is certainly of significance.

Subsequent determinations by similar methods have been made on 18 women whose chief complaint was menorrhagia or who were admitted to the hospital with a hypochromic anemia which seemed to be due in part to an abnormal menstrual loss even though they themselves considered their menses to be normal. This brief report is merely a presentation of these findings for the purpose of recording the amount of blood and hemoglobin which is actually lost under such circumstances.

The amount of hemoglobin is the most accurate method of presentation of these data, whereas if this is expressed in terms of cubic centimeters of blood, it does not give the essential information because the results vary with the blood hemoglobin values. For example, the loss of 5 gm. of hemoglobin will represent from 33 to 100 c.c. of blood, depending on whether the patient had 15 or 5 gm. of hemoglobin per 100 c.c. of circulating blood.

METHODS

Cellulocotton pads were utilized for the collection of the menstrual flow and the material was analyzed for iron by a modification of the method of Reis and Chakmakjian.[2] The iron was converted to its equivalent in grams of hemoglobin, and this in turn to cubic centimeters of the patient's blood. Table I gives the essential data for each patient with their menstrual loss in terms of iron, hemoglobin, and blood. The duration of the menstrual flow and the number of napkins used are likewise recorded. Table II gives the results on 5 patients on whom more than one observation was made. We believe that all these results must be considered as abnormal since they are above the average value as determined in the preceding study, although not all are above the highest values encountered in that group.

Several cases are included in which the diagnosis of idiopathic hypochromic anemia was made. We believe this form of anemia is primarily a chronic hemorrhagic anemia occurring in a patient who is unable to properly metabolize the dietary iron.[3] Most of these patients had not recognized that they were losing an abnormally large amount of menstrual blood.

*Supported in part by a grant from the Eli Lilly Co.

TABLE I. MENSTRUAL BLOOD LOSS

CASE	AGE	BLOOD			DURATION OF PERIOD DAYS	NUMBER OF NAPKINS USED	MENSTRUAL LOSS			DIAGNOSIS
		R.B.C. MILLIONS	HEMAT. %	HB. GM.			IRON MG.	HB. GM.	BLOOD C.C.	
1	34	4.48	31.0	6.14	2 days	4	20.57	7.14	116.28	Idiopathic hypochromic anemia
2	34	3.85	33.0	7.10	7 days	20	25.02	7.47	105.21	Menorrhagia
3	33	3.54	24.0	4.61	2 days	4	30.50	9.10	197.18	Hematuria and hypochromic anemia
4	50	4.64	35.0	10.71	3 days	6	33.75	10.07	94.02	Climacteric bleeding
5	24	4.47	34.5	9.47	8 days	16	44.80	13.37	141.21	Menorrhagia
6	40	3.63	29.0	6.20	7 days	43	47.38	14.14	228.06	Idiopathic hypochromic anemia
7	37	4.77	34.0	6.46	7 days	25	49.59	14.80	229.12	Idiopathic hypochromic anemia
8	44	4.07	28.0	6.26	5 days	21	53.42	15.94	254.31	Idiopathic hypochromic anemia
9	25	4.52	36.0	10.90	3 days	10	59.73	17.82	163.48	Idiopathic hypochromic anemia
10	42	3.97	36.0	10.22	9 days	38	95.60	28.54	279.22	Leiomyoma
11	26	3.83	27.0	10.10	4 days	23	96.47	28.79	285.04	Menorrhagia
12	35	3.88	20.5	4.72	5 days	7	145.89	43.54	922.45	Idiopathic hypochromic anemia
13	48	4.19	38.0	7.19	6 days	36	146.36	43.65	607.09	Menorrhagia
14	23	3.93	32.0	7.89	22 days	65	153.69	45.87	581.37	Incomplete abortion
15	41	4.33	26.0	11.80	5 days	13	163.00	48.65	412.29	Idiopathic hypochromic anemia
16	40	4.75	38.0	12.01	5 days	20	182.07	54.36	452.42	Idiopathic hypochromic anemia
17	33	3.68	33.0	9.02	9 days	58	207.80	62.03	687.68	Fibromyoma
18	45		38.0	11.36	6 days	39	220.15	65.72	578.48	Menorrhagia

RESULTS

The hemoglobin lost per menstrual period in these 18 cases varied from 7 14 to 65.72 gm. This represented a loss of from 94.02 to 922.45 c.c. of the patient's blood, as calculated from their actual blood hemoglobin. The degree of anemia did not parallel the amount of blood lost.

TABLE II. VARIATIONS IN THE MENSTRUAL BLOOD LOSS IN THE SAME INDIVIDUAL

CASE	AGE	BLOOD			MENSTRUAL LOSS			DIAGNOSIS
		R. B. C. MILLIONS	HEMAT. %	HB. GM.	IRON MG.	HB. GM.	BLOOD C.C.	
5	24	4.73	36.0	10.73	38.00	11.34	105.71	Menorrhagia
		4.47	34.5	9.47	44.80	13.37	141.21	
10	42	4.52	36.0	11.29	78.40	23.40	207.28	Leiomyoma
		3.97	36.0	10.22	95.60	28.54	279.22	
15	41	4.44	41.0	12.63	100.40	29.97	237.39	Idiopathic hypochromic anemia
		4.33	26.0	11.80	163.00	48.65	412.29	
16	41	4.15	33.0	7.36	50.62	15.11	205.15	Idiopathic hypochromic anemia
		4.75	38.0	12.01	182.07	54.36	452.42	
18	46	3.79	31.5	7.71	186.29	55.61	720.79	Menorrhagia
			38.0	11.36	220.15	65.72	578.48	

In Table II are presented those cases in which more than one observation was made. These are numbered to correspond to their position in the preceding table in which the period with the greater loss is given. It will be noted in Cases 5 and 10 that the variation was not great, whereas in the other 3 cases, and particularly in Case 16, there is a great variation from one period to the other.

We have been unable to find reports of a similar nature in the literature except that of Hoppe-Seyler[4] who analyzed the menstrual loss in 15 women. In 4 normal cases the average loss was 37 c.c. of blood, while in the 11 abnormal ones the loss ranged upward to 376 c.c.

COMMENT

Although no very definite limits of the normal menstrual blood loss can be set, we present these results as representative of abnormal menstruation. Not all of the patients appreciated the fact that their periods were more profuse than the average. Even the patient (Case 12) who lost 43.54 gm. of hemoglobin, or 922.45 c.c. of blood, stated that her menses were not profuse. Since these individuals have no means of comparison, it is obvious that one cannot rely on their statement as to the normalcy of their menses.

No definite conclusions can be drawn from these results as to the amount of blood lost in individual cases of menorrhagia, and the data are presented merely as accurate measurements in certain pathologic cases.

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AN APPARATUS FOR PROCURING ESSENTIAL DATA IN THE DIFFERENTIAL DIAGNOSIS OF PELVIC PATHOLOGY IN THE FEMALE*

GEORGE LYFORD, M.D., CINCINNATI, OHIO

(From the Department of Gynecology, College of Medicine, University of Cincinnati)

DURING the past fifteen years or so in which transuterine insufflation has been increasingly used for the study of the Fallopian tubes, much has been written of its diagnostic value, its dangers, and its use as a therapeutic agent. Theoretically, at least, it would seem that this method could also be used for studies of the normal physiology, and this to some extent has been attempted.

One of the fundamental difficulties encountered in such studies has been the inaccuracy of the apparatus. Another of almost equal importance has been the discomfort to the patient resulting from the insufflation. It was in an attempt to overcome these difficulties that our first apparatus was devised.

The general structure of the apparatus can be seen in Fig. 1. It consists of: a source of gas and pressure, the smallest available tank of carbon dioxide; a graduated cylinder and plunger to contain the gas used during the procedure, above which is a pressure reservoir by which the plunger may be forced into the cylinder; a mercury manometer for the gross measurement of pressure which is connected, by means of a float and stylus, for the recording and accurate measuring of pressure; an exhaust valve for immediately exhausting the entire system; a safety valve to maintain a given predetermined pressure in the entire system, adjustable from zero to 220 mm.

In operating the apparatus the safety valve is first adjusted by elevating or lowering the mercury container, in which rests the tube connected to the gas line between its source, the tank, and the remainder of the apparatus. This pressure on the first examination should obviously not exceed the normal pressure, 100 to 120 mm., subsequent pressures to be determined by the findings on the first examination. The valve of the gas tank is then opened, the flow being roughly controlled by a needle valve, to supply a constant stream of bubbles through the mercury safety valve. The gas is then turned into the graduated cylinder filling it to the required volume, which our experience so far has shown us to not exceed 25 c.c. By now shunting

*A paper on the clinical value of the uterosalpingogram ("The Utero-Salpingogram as a Means of Differential Diagnosis in Gynecological Pathology." J. Med. Cincinnati, Ohio, Nov., 1936.) was followed by many requests for an explanation of the technique and apparatus used. Before discussing this, however, I should like to express my appreciation for the invaluable cooperation of Dr. T. J. LeBlanc, Professor of Preventive Medicine, in the development of the original equipment and of the work of W. E. Stilwell, Jr., in the building of our present apparatus, and to Drs. H. G. Reineke, William Doughty, and E. R. Bader, Department of Radiology, for their assistance in the x-ray phase of the study.

the gas into the pressure chamber above the plunger, a pressure can be exerted upon the gas in the cylinder equal to, but never exceeding, the pressure at which the mercury safety valve has been set. When it is desired to insufflate, the needle control valve between the graduated cylinder and the manometer is slowly opened, allowing the gas to escape through the tube into the uterine cannula; the manometer and recording apparatus, being shunted in parallel with this side of the system, will fluctuate with any changes in pressure. When the desired results have been obtained, the exhaust valve is turned, exhausting the uterine side of the apparatus instantaneously.

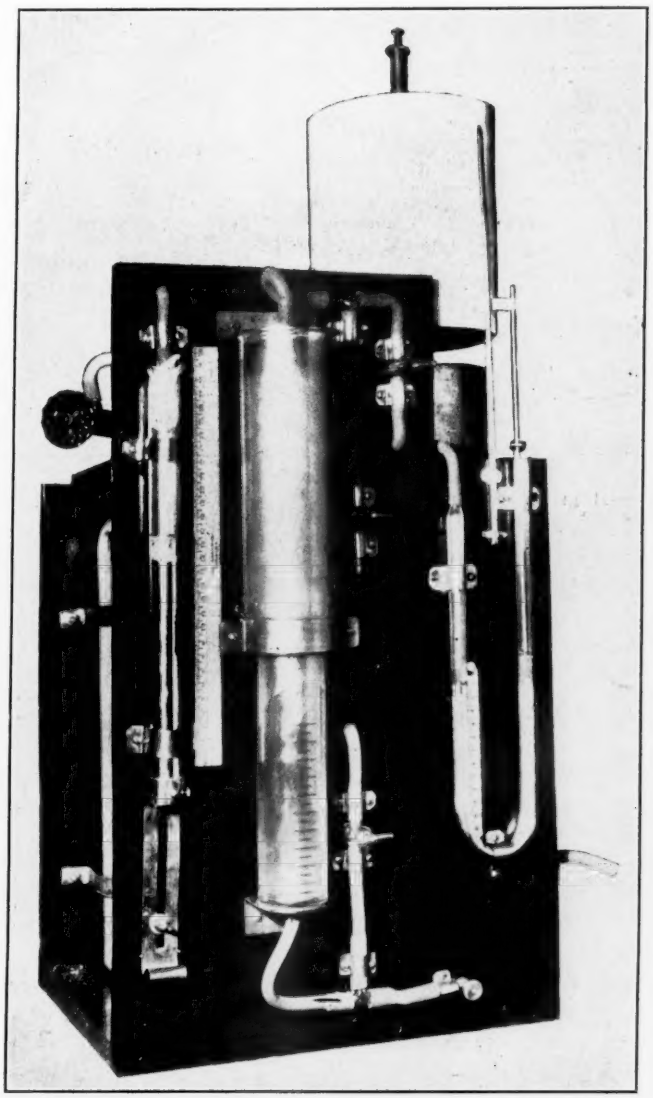

Fig. 1.—Original apparatus.

From the 2,783 insufflations for which this apparatus has so far been used, we draw the following observations. Though there may be occasional discomfort in the region of an opening tube, it is of short duration, relieved by exhausting the apparatus, and it is very seldom followed by subphrenic referred pain, which, though of diagnostic value,

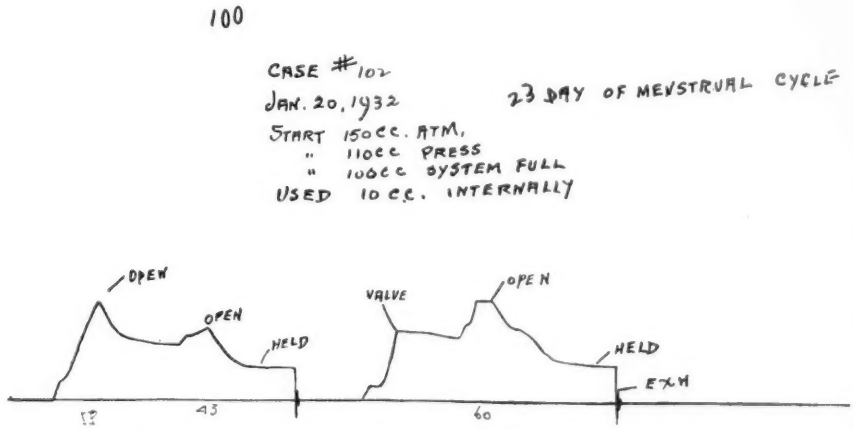

Fig. 2.—Normal graph showing the relatively sharp opening, fall in pressure, and gradual reduction.

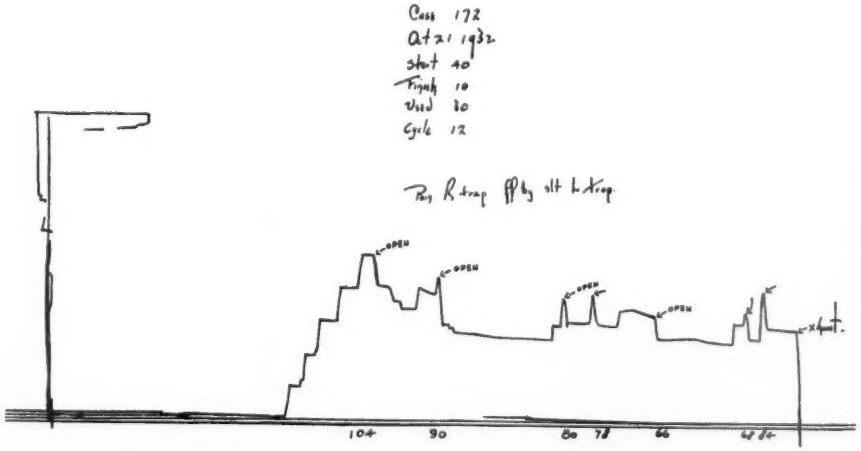

Fig. 3.—Dysmenorrhea showing the spasmodic response, gradual reduction over all by frequent marked elevations followed immediately by an acute fall, the average remaining normal or high.

is not necessary. It has not been necessary for patients to rest following the insufflation, since they are able to continue their activities immediately. The recording apparatus, as checked against an independent manometer, has an inaccuracy never to exceed 1 mm. in 200. The volume required has so far never exceeded 25 c.c., even when repeated checks have been made at one sitting and can be read or estimated within 1 c.c.

The exhaust requires by stop watch timing two seconds to evacuate the uterine side of the apparatus, a slight negative pressure being produced which probably accounts for the immediate cessation of symptoms.

The accompanying graphs (Figs. 2, 3, and 4) illustrate a few of the changes occurring both in apparently normal and in abnormal tubes with reference to phases in the menstrual cycle, dysmenorrhea, etc. The group is not sufficiently large, as the majority have been sterility cases, to permit of analysis, certainly not of conclusions at the present time, but is constantly increasing. It will also be noted that the apparatus is extremely sensitive and extraneous influences must be carefully controlled by the operator. It has also been found that due to the ease

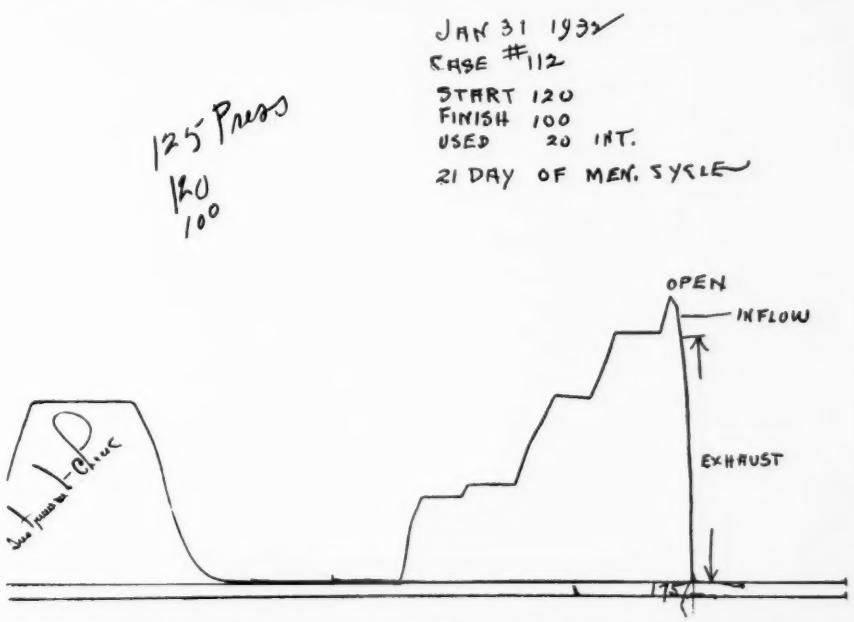

Fig. 4.—Partial tubal obstruction: a rather typical picture of the strictured or partially occluded tube, opened by gradually increased pressure and volume as the steps on the curve show. (Sterility due to mechanical obstruction successfully relieved by repeated dilatation by insufflation.)

of control and adaptability of the apparatus, an entire set of graphs can be made and checked in fifteen minutes or less with no discomfort to the patient.

Since the above described apparatus was completed (1931) and very satisfactorily used in well over a thousand cases, an apparatus was constructed, working on the same principles, but so controlled electrically as to be automatic, compact, and include a method of injecting opaque oil.

It includes the following features described in detail below: (1) gas pressure starts from zero and is gradually increased rather than being reduced from the

highest pressure; (2) the patient and the apparatus are automatically disconnected (a) when the reservoir pressure approaches zero, (b) when the pressure within the patient is reduced as a result of opening of the tube, leakage, etc., and (c) when the pressure within the patient has reached a predetermined maximum; (3) a graphic record is made which is accurately synchronized as to time and pressure for gas and oil; (4) it contains a maximum pressure regulator, adjustable from zero to 300 mm.; (5) the lighting of the dials is so arranged as to permit dimming below the point of objection for use during fluoroscopy, still allowing visibility; during the use of the apparatus the red and green lights are a constant indicator to the operator as to whether the patient is or is not connected; (6) remote control—the entire control of the apparatus is by means of a single hand switch on a cord of any length convenient, thus permitting the operator to be at any distance from

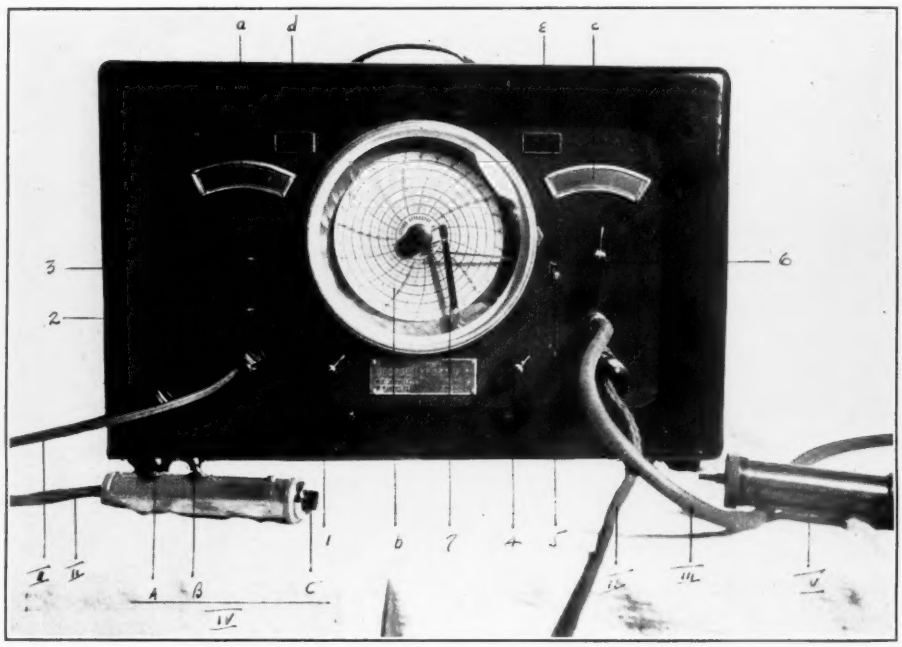

Fig. 5.—Front view of apparatus.

the apparatus during manipulations within the patient; (7) the oil reservoir permitting the instillation of opaque oil under the controlled gas pressure of the apparatus with a graphic record; (8) a gas filter; (9) an attachment permitting the use of compressed gasses, this is attached at the head of the gas filter as a lead to the tank of compressed gas, if such a tank is used it must be equipped with a reducing valve; (10) built so compactly as to be portable.

In Fig. 5 is shown the control panel: *a*, finger dial indicator of the gas pressure within the reservoir; *b*, a rotating chart dial graphically representing time and pressure connected, as later described, for the automatic cut-out at reduced intrauterine pressure or maximum pressure; *c*, a finger indicator dial for maximum pressure, adjustable from 0 to 300 mm.; *d*, green light; *e*, red light; *1*, the switch to turn on current from wall plug; *2* and *3*, switches to control intensity of illumination of dials; *4*, switch controlling the rotation of the graphic chart, *b*; *5*, adjust-

ment lever for stylus, *7*; *6*, knob for adjusting maximum pressure control: *I*, Lead from source of electrical supply; *II*, remote control lead; *III*, tube leading to cannula within the patient with male and female Luer fittings; *IV*, hand control (remote control)—*A*, switch for manually disconnecting apparatus from patient by operating the mechanism controlling valve in the line to the patient; *B*, switch for operating contact mechanism; *C*, button controlling operation of motor-compressor unit; *V*, oil reservoir-cartridge for instillation of opaque oil.

Fig. 6 is a view of the apparatus with the back of the cabinet removed.

PROCEDURE

The uterine cannula is placed in or through the cervix with the usual technique for insufflations, using surgical care for antisepsis. The patient is then placed in a slight Trendelenburg position and the vagina filled with a mild antiseptic solution

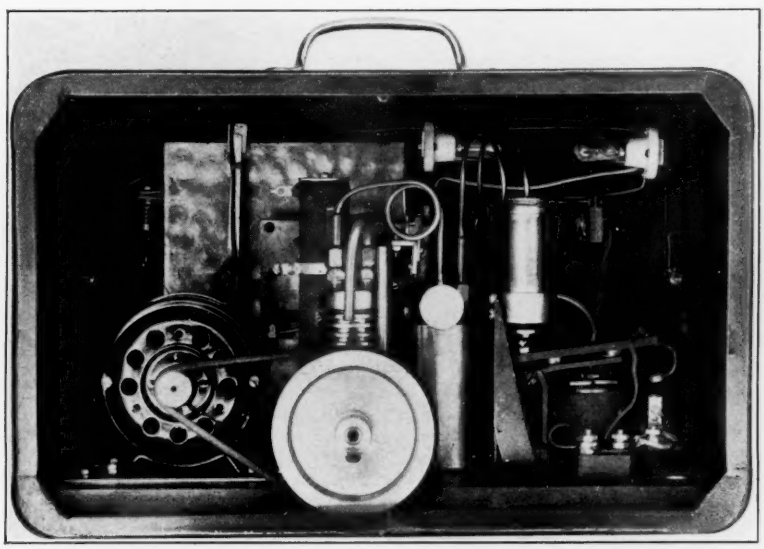

Fig. 6.—Rear view of apparatus.

making a "water seal"; the cannula is connected with the apparatus by means of the flexible gas tube with Luer fittings (Fig. 5, *III*); switch *1*, Fig. 5, is turned for a current supply; switches *2* and *3* are turned as needed for the control of the light intensity on the dials; switch *4*, Fig. 5, is turned to start the recording chart *b*, Fig. 5, rotating; lever *5*, Fig. 5, is adjusted so the stylus *7* makes a tracing on the chart; switch *6* is turned to set the indicator at the maximum pressure beyond which it is not desired to have the apparatus operating at a given time.

By pressure on the button of the remote control *IV*, *C*, Fig. 5, the motor-compressor starts operating, building a reserve pressure in reservoir indicated on dial *a*, Fig. 5. The switch *IV*, *B*, on the remote control is then turned making contact through the mechanism regulated by the stylus arm operating the control valve in the line to the patient. At this point the green light *d* goes off and the red light *e* comes on. When the gas has started flowing through the cannula, the remote control switch *IV*, *B* is turned to its original position and the red light continues glowing; however, if this switch is thrown before gas is actually flowing through the

valve and cannula, a "disconnect" occurs, the red light goes off and the green light comes on. If the latter occurs, the switch is again thrown, this time for a longer period. This flow of gas can also be noted on the recording chart, since the stylus will gradually rise as the gas increases the intrauterine pressure. The procedure is continued by running the compressor sufficiently to maintain a gas pressure in the reservoir as indicated on dial *a* in Fig. 5. Under ordinary circumstances for insufflation, a reservoir pressure of around 200 mm. is more than adequate. Dial *a* indicates *only* the pressure in the reservoir and has no significance as to the intrauterine pressure which is indicated on chart *b* only.

When gas escapes from either or both of the Fallopian tubes, or when the maximum pressure, previously adjusted on dial *c*, Fig. 5, is reached, the apparatus is

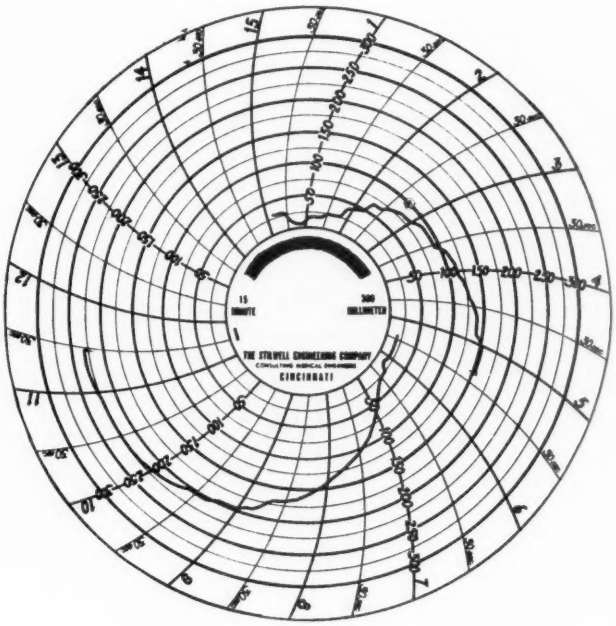

Fig. 7.

automatically disconnected from the patient, as explained above. Leakage around the cannula, of course, is noted by bubbling through the "water seal," by a "disconnect," or by both.

When an x-ray examination with opaque media is to be done, the procedure is the same as outlined above, except that the oil cartridge *V* is inserted between the uterine cannula and the end of the flexible tube, and the maximum pressure control is raised 150 mm. above insufflation opening. (This is the approximate oil resistance. This figure can be obtained in any given instance by determining at what pressure oil starts flowing through the cannula before its insertion into the uterus.) The gas pressure is then gradually increased, as with insufflation, the oil noted under the fluoroscope as it enters the uterus and tubes, and films made as indicated. This fluoroscopy and films can then be checked with the graphic record on the chart.

Our usual procedure is to do an insufflation and immediately follow it with x-ray without moving the patient from the table, since the roentgenologic findings

are of paramount importance, and unless contraindicated, should always be done for diagnoses, although not always necessary in follow-up therapy.

The graphic chart (Fig. 7) shows the curve of increase in transuterine pressure with gas, with its abrupt fall when the tube opens; followed by a curve of the gradually increasing pressure during the oil instillation for fluoroscopy and x-ray. Note that the chart records the time factor of flow, as well as pressure, and from these can be computed the relative gas volume used.

The x-ray plate of the uterosalpingogram corresponding with the chart curve of Fig. 7 is shown in Fig. 8. A comparison of these two with timing permits the interpretation of the rate of flow, etc., from which the diagnoses are made.

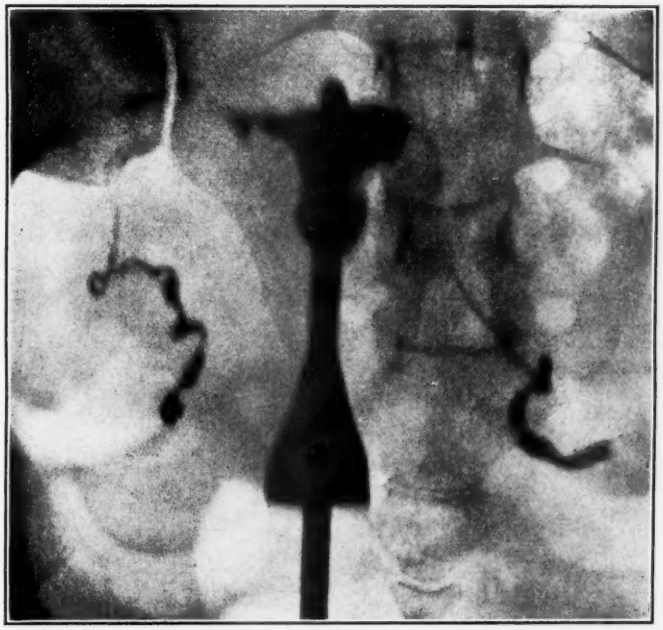

Fig. 8.—Uterosalpingogram of patient shown in curve of Fig. 7.

SUMMARY

An apparatus has been developed which permits of an automatic control of the maximum pressure of gas within the uterus with automatic safety factors well within the danger limit. This apparatus also permits of controlled instillation of opaque oils for x-ray study of pelvic pathology. These procedures are regulated by a simple hand-switch carried by the operator. The apparatus produces an accurate graphic record of time and pressure both of gas and oil.

CONCLUSIONS

Reviewing 393 examinations for which the latter apparatus has been used, the following tentative conclusions have been drawn:

1. The disconnect apparatus, being electrically controlled, is practically instantaneous in its response.

2. The synchronization of the contact and control mechanism with the hand switch has a sufficient latent period to make it impossible to start a flow of gas without conscientious concentration on the part of the operator.

3. The hand control permits free movement of the operator at any convenient distance from the apparatus with absolute control of the apparatus, even to immediate disconnection if indicated.

4. The flow of gas and oil is so sufficiently slow and regular that the patient has no subjective symptoms other than an occasional sensation of fullness and is able to be up and about immediately following the manipulation.

5. By *deliberately* setting the various control switches, it is possible, if desired, to continue the flow of gas or oil ad lib. if a pneumoperitoneum, etc., is desired. (Note the emphasis on deliberate.)

6. The data obtained from the use of this apparatus, gas pressure, x-ray, etc., we have found of great value in the differential diagnosis of female pelvic pathology by no means limited to the study of the problem of sterility.

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809 Carew Tower

Haselhorst, G.: A Single Mishap in Tubal Sterilization in the Female, Zentralbl. f. Gynäk. **61:** 306, 1937.

Haselhorst has employed the method of crushing the Fallopian tubes in 170 women as a means of sterilization. Thirty-five of them were subsequently investigated radiologically; one woman had one patent Fallopian tube. He has found this method simple and effective on nonpregnant women but definitely unreliable when it is combined with evacuation of a pregnant uterus, or for the treatment of a patient during the puerperium. The writer contradicts the suggestion made by Hartmann, that he only aims at the destruction of the peristaltic tubal action without obliteration of the lumen. He considers it essential to destroy the whole tubal wall except the peritoneum when crushing the tube.

J. P. Greenhill.

AMPLIFICATION OF FETAL HEART SOUNDS*

W. T. Pommerenke, M.D., and Francis W. Bishop, Rochester, N. Y.
(From the Departments of Obstetrics and Gynecology, and Medicine, Division of Radiology, of the University of Rochester School of Medicine and Dentistry)

THE ability to perceive fetal heart sounds provides impeccable evidence not only of pregnancy but also of fetal life. Auscultation, moreover, furnishes confirmatory evidence concerning the presentation and position of the fetus, and may be helpful in the detection of a multiple pregnancy. More important, it provides one of the few reliable means of recognizing impending peril to the life of the fetus, as during a prolonged and difficult labor, or one which is associated with hemorrhage. Its usefulness is apparent in the diagnosing of a suspected stillbirth. One will not infrequently be called upon to select a mode of delivery when the prudent decision will be dependent upon the establishment beyond peradventure of the well being or death of the fetus. Lack of exact information on this point may lead to tragic diagnostic error. The characteristics of the fetal heart sounds may foretell threatening asphyxia and demand immediate operative delivery by means of which an otherwise hopelessly doomed child may be rescued. Seldom indeed would one be required to do a destructive operation on a living child. Moreover, when death of the fetus is once recognized, advised conservative care of the mother becomes the only important consideration; and her interests may often then best be served if deliberation supplants haste.

Whereas Fasbender[1] ascribes the first audition of fetal heart sounds to LeGoust in 1650, others[2, 3] record that these sounds were first heard by Mayor[4] of Geneva in 1818. This was two years after Laennec's[5] discovery of the stethoscope. Unaware of Mayor's disclosure, Kegaradec[6] in 1822 also heard the sounds of the fetal heart and described these in his classical monograph with such completeness that many years passed before significant additions were made to his accounts. DePaul,[7] who claimed to have heard the fetal heart during the eleventh week of uterogestation, in 1847 suggested auscultation as an aid in determining the position of the fetus. In 1907 Einthoven[8] applied the capillary electrometer as a means of registering and analyzing heart sounds. Williams[9] in 1921 converted sound oscillations into electrical oscillations by means of an electromagnetic transmitter and used a string galvanometer to graphically record heart murmurs.

Unfortunately, the fetal heart sounds are infrequently audible before the sixteenth to twentieth week of pregnancy. Even after this time, adverse conditions may render satisfactory auscultation difficult. Among these conditions may be cited: (1) An obese abdominal wall; (2) an excessive amount of amniotic fluid; (3) an unfavorable posi-

*Received for publication, June 22, 1937.

tion of the fetal thorax with reference to the mother's abdominal wall; and (4) the presence of adventitious sounds. Furthermore, just prior to actual delivery the accoucheur is frequently dependent for the interpretation of the fetal heart sounds upon an assistant or nurse who may encounter delay in locating them, and in so doing may cause disheveled ment of the sterile drapes. This may be especially annoying with a distraught or difficult patient.

To obviate some of these undesirable features and conditions, the thought occurred to us that with modern electrical equipment one might be able to amplify the fetal heart tones with an intensity and fidelity heretofore difficult to obtain. The use of the vacuum tube amplifier in connection with the auscultation of clinical sounds is not new.

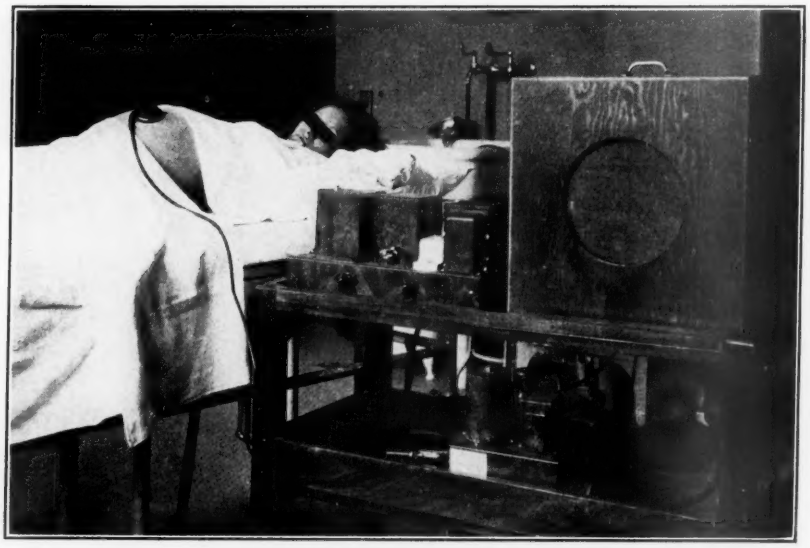

Fig. 1.—Photograph showing the apparatus in operation. The portable feature allows the amplifier to be placed in an adjacent room.

Squier[10] in 1921 demonstrated the practicability of amplifying the adult heart sounds with such a method. Abbott[11] in 1922 described an amplifying device that enabled hundreds of persons in a large room to hear the heart sounds with the aid of a loud speaker, and according to Keiper,[12] a similar device has been used to demonstrate the fetal heart sounds. Jacobsohn[13] suggested the use of the vacuum tube in obstetrics. Gamble and Replogle[14] were able to reproduce fetal heart sounds on a loud speaker by means of a mechanism described by them and by Cabot.[15]

In our opinion, the potential value of a device for the amplification of the fetal heart sounds has not been generally appreciated nor sufficiently emphasized. That this is true is not surprising when one considers that heretofore, and for the most part, suitable equipment has been costly, bulky, and cumbersome. Likewise, for years technical difficulties made reception of sounds unsatisfactory. More recent develop-

ments of the radio arts have produced small and relatively inexpensive high gain AC operated amplifiers with a very low hum level and large power output. Such an outfit was made available to us, and upon actual test we were able with it to hear the fetal heart sounds with good room volume, clarity, and freedom from many of the distortions and difficulties that had previously beset efforts to satisfactorily amplify the sounds.

DESCRIPTION OF APPARATUS

The amplifying equipment consists of a stock Stromberg-Carlson AC operated 11-A amplifier in conjunction with their No. 13 Universal amplifier. This combination has a total gain of 108 decibels with a frequency response flat with less than 3 DB total variation from 30 to 10,000 cycles per second. The amplifier is capable of 12½

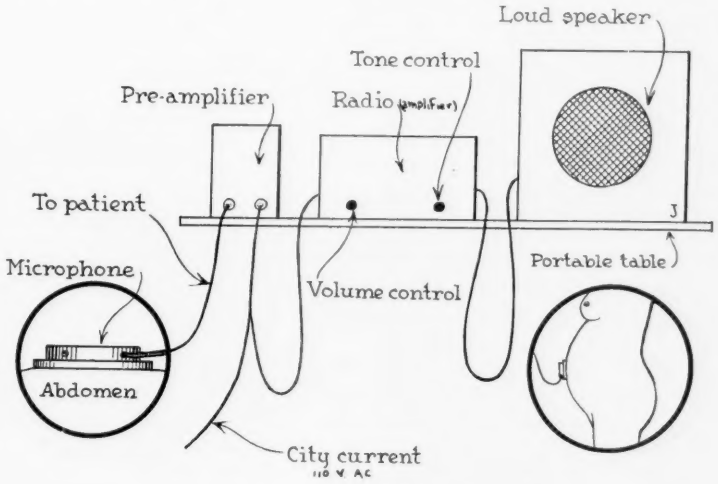

Fig. 2.—Schematic diagram of apparatus.

watts output or +33.2 DB when zero level is taken as 0.006 watts, with less than 5 per cent harmonics. The hum level is at least 50 DB below maximum output. A modified earphone of an impedance to match the preamplifier serves as the microphone or pick-up, and is placed over the point of maximal impulse of the fetal heart. The diaphragm has been made free floating to improve the low frequency response. The labor and delivery rooms are all acoustically treated and permit the use of the loud speaker in the same room as the microphone, at fairly high volume levels, without acoustic feedback. We have been able to obtain sufficient output from the amplifier, with the fetal heart sounds, to cut satisfactory phonograph discs, using the new acetate records common in electrical transcriptions for radio purposes.

This recording equipment is being used as a means of preserving the heart sounds in unusual cases and to build up a library of discs for teaching purposes, and will be described in another paper. It is hoped that these devices will aid in clinical instruction. Since the fetal pulse is very labile, continuous auscultation of the heart gives much more accurate information of the true state of affairs than is possible with

the usual methods of examination. After following the vagaries of a given fetal heart during the time preceding delivery, one learns what to expect by way of variations and may thus eliminate one source of anxiety.

Although we have applied this equipment only to a comparatively small series of normal cases, we believe that its practical utility in diagnosis is apparent. The ease with which the microphone can be retained in position facilitates repeated examination and precludes the inconvenience of a disturbing feature concerned with repeated exposure of the patient. And if a prediction is allowable, we believe that this general method will prove useful in gaining further information relating to physiologic and pharmacologic influences on the fetal heart.

We wish to acknowledge the technical assistance and cooperation rendered by Dr. Ray Manson, Mr. Fred Young, and Mr. Oliver Angevine. The equipment was provided by the Stromberg Carlson Telephone Manufacturing Co.

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Wolff, Ulrich: Practical Hints for the Obstetrician, München. med. Wchnschr. **83**: 1868, 1936.

For completing a miscarriage the curette is not dangerous provided the cervix has been adequately dilated and the principal mass is removed with a large blunt curette. Prophylactic immunization with Streptoserin was found very valuable in cases of infected abortions.

In cases of habitual abortion, Proluton is injected weekly after the sixth week for a period of 4 to 5 months.

A diet during pregnancy, especially during the last two months, which includes very little milk and practically no meat tends to prevent oversized babies and more serious metabolic disturbances.

Wolff recommends bag induction of premature labor.

Walcher's position furthers entrance of the fetal head into the inlet, especially in the case of a flat rachitic pelvis.

The parturient's position, especially on the side, influences rotation and causes a particular portion of the head to descend lower.

C. E. PROSHEK.

CORRELATION BETWEEN BLOOD PRESSURE AND NEMBUTAL DOSAGE IN THE TOXEMIAS OF LATE PREGNANCY

JULIAN WALDO ROSS, M.D., WASHINGTON, D.C.

(From the Department of Obstetrics and Gynecology, Howard University School of Medicine and Freedmen's Hospital)

HIGH blood pressure (140 systolic or above) is generally the first and most reliable clinical finding to signify the advent of the toxemias after the twentieth week. Similarly a high and rising blood pressure indicates increasing toxemia which if not checked may terminate in convulsions, uteroplacental apoplexy, cerebral hemorrhage, or death; all obstetric calamities.

In this report is presented a dosimetric schedule based on the height of the blood pressure, using nembutal as our basic therapeutic agent.

METHOD

The following plan was devised. Our cases were divided into 6 groups according to the blood pressure heights and treated with nembutal, put up in 1½ gr. (90 mg.) capsules, in graded doses per os:

Group I, with blood pressure of 140 to 149, received 1 capsule q.i.d.

Group II, with blood pressure of 150 to 159, 2 capsules, t.i.d.

Group III, with blood pressure of 160 to 169, 3 capsules, t.i.d.

Group IV, with blood pressure of 170 to 179, 3 capsules, q.i.d.

Group V, with blood pressure of 180 to 189, 3 capsules 4 to 5 times daily.

Group VI, 190 and above, venesection plus 2 to 3 capsules 3 to 4 times daily.

The standard dosages were modified subject to individual responses within each group (see type cases). The prevalent measures of combating pregnancy toxemias were used concurrently with this dosimetric method.

Sixty cases of late pregnancy toxemias in our series during the past two years were treated in accordance with the above schedule and not one developed any of the above obstetric calamities. In the selection of our cases, those with preexisting hyperpiesis and/or chronic glomerulonephritis were not included.

The following six cases may serve as typical of the reactions of each of the corresponding groups, respectively:

Group I.—Blood pressure 144/100. B. S., aged nineteen years, para 0, admitted not in labor May 13, 1937; referred to hospital by Welfare Clinic because of severe headaches, edema of face, eyes, and lower extremities, and albuminuria of several weeks' duration; albumin plus 4, sedimentation 30 mm. in fifty minutes, eye grounds negative, Wassermann negative, nembutal capsules one q.i.d.

5/13/37—Patient admitted
5/14/37—Blood pressure 146/100
5/15/37—Blood pressure 170/120, three capsules q.i.d. as pressure progressed into Group IV
5/17/37—Blood pressure 170/120, labor set in and delivery of premature (seven months) live infant; following delivery, pressure dropped to 130/100
5/18/37—Blood pressure 137/70, nembutal discontinued, edema gone, high colonic irrigations once daily with low protein diet
5/20/37—Blood pressure 126/88
5/22/37—Blood pressure 118/70
5/24/37—Blood pressure 118/78
5/25/37—Blood pressure normal, sedimentation 15 mm. in one hour, patient discharged in good condition

Group II.—Blood pressure 150/100. B. T., aged sixteen years, para 0, admitted to hospital May 6, 1937, not in labor. Complained of occasional headaches and edema of eyelids, albumin plus 2, sedimentation 33 mm. in 25 minutes, eye grounds negative, nembutal capsules two t.i.d.

5/ 6/37—Patient admitted
5/ 7/37—Blood pressure 154/100
5/ 8/37—Blood pressure 140/90
5/ 9/37—Blood pressure 138/90, edema gone
5/10/37—Blood pressure 140/90, labor began
5/12/37—Blood pressure 130/90, delivered full-term live infant, nembutal discontinued
5/14/37—Blood pressure 110/60
5/15/37—Blood pressure 104/68, albumin negative
5/18/37—Blood pressure 100/60, patient discharged in good condition

Group III.—Blood pressure 166/128. I. F., aged nineteen years, para 0, admitted not in labor Feb. 24, 1936, from prenatal clinic because of rising blood, pressure, severe headaches and impaired vision, albumin negative, sedimentation 28 mm. in one hour, eye grounds negative. Wassermann plus 4, phenolsulphonephthalein 55 per cent in two hours, blood urea clearance 58 per cent (Cs), nembutal capsules two b.i.d.

2/24/36—Patient admitted
2/25/36—Blood pressure 188/144, two capsules t.i.d. as pressure is rising

2/27/36—Blood pressure 166/134
2/28/36—Blood pressure 164/130
2/29/36—Blood pressure 162/126, 158/120
3/ 1/36—Blood pressure 158/122
3/ 4/36—Blood pressure 150/118
3/ 7/36—Blood pressure 188/130, labor set in, albumin plus 4, hyaline and granular casts and pus cells
3/ 8/36—Blood pressure 210/132, and delivery of premature live infant
3/ 9/36—Blood pressure 180/120
3/11/36—Blood pressure 154/110
3/12/36—Blood pressure 138/100
3/14/36—Blood pressure 128/92, nembutal discontinued
3/16/36—Blood pressure 124/80
3/19/36—Blood pressure 120/80, patient discharged in good condition

This case did not receive the full scheduled dosage of nembutal as antisyphilitic treatment was given concurrently; however, there was a gradual decline in blood pressure to normal.

GROUP IV.—Blood pressure 170/100. M. D., aged thirty-one years, para 0, admitted in labor Aug. 9, 1936, with edema of legs and delusions of design on her life by her people and persecution, albumin plus 4, sedimentation 32 mm. in one hour, eye grounds negative, Wassermann negative, Fouchet test positive in 5 min., phenolsulphonephthalein 55 per cent total output, nembutal given as per schedule.

8/ 9/36—Patient admitted; 2 hours after admission pressure 192/112; 5 hours after admission blood pressure 210/100; venesection of 500 c.c. of blood plus scheduled use of nembutal
8/10/36—Delivered stillborn infant at term
8/11/36—Blood pressure 165/100
8/13/36—Blood pressure 152/94, edema gone
8/16/36—Blood pressure 122/84, nembutal discontinued
8/20/36—Blood pressure 100/80
9/ 7/36—Sedimentation 13 mm. in one hour
9/ 8/36—Mentally clear
9/11/36—Fouchet test negative
9/20/36—Blood pressure 105/75, patient discharged in good condition

GROUP V.—Blood pressure 184/100. E. R., aged thirty-six years, para 0, admitted Aug. 24, 1936, having had 4 convulsions, albumin plus 4, sedimentation 26 mm. in one hour, eye grounds negative, Wassermann plus 4, edema of face, hands and feet, mental confusions, phenolsulphonephthalein 65 per cent total output, nembutal given per schedule. No further convulsions.

8/24/36—Patient admitted
8/26/36—Blood pressure 136/98, mentality clear
8/28/36—Blood pressure 140/86
8/30/36—Blood pressure 166/100, in labor, edema gone

8/31/36—Blood pressure 176/106, delivered a stillborn fetus, albumin 3 plus
9/ 1/36—Blood pressure 118/102, nembutal stopped
9/ 5/36—Blood pressure 118/102
9/13/36—Blood pressure 120/90, Fouchet 14 mm. in one hour, albumin plus 2, patient discharged in good condition

GROUP VI.—Blood pressure 190/130. A. P., aged sixteen years, para 0, admitted June 17, 1936, complaining of shortness of breath, dizziness, edema of ankles, albumin plus 4, eye grounds negative, Fouchet negative, nembutal capsules one t.i.d. until delivery June 19, and 5 capsules during delivery, then discontinued, all contrary to orders.

6/17/36—Patient admitted
6/18/36—Blood pressure 172/120
6/19/36—Blood pressure 206/140, delivered full-term live infant
6/20/36—Blood pressure 186/106
6/22/36—Blood pressure 248/128, 2 convulsions, albumin one-plus, nembutal 2 capsules intravenously and 8 capsules per os. The dosimetric schedule started. No further convulsions which in the first place might have been prevented had the treatment plan been instituted from the beginning and followed through
6/23/36—Blood pressure 210/122
6/24/36—Blood pressure 186/120
6/25/36—Blood pressure 172/116
6/26/36—Blood pressure 155/110
6/27/36—Blood pressure 144/96
6/28/36—Blood pressure 140/100
6/29/36—Blood pressure 135/90
6/30/36—Blood pressure 130/85, patient discharged in good condition

This case was especially selected from its group to emphasize the importance of rigorous adherence to the method advocated in order to make certain the eliciting of the anticipated results.

DISCUSSION

From the study on these cases of the correlative action of nembutal and response of the high blood pressure in the treatment of the late pregnancy toxemias, we are led to believe that a high and rising blood pressure is a reliable index of the degree of the toxemia. The high blood pressure was markedly reduced towards normal following the use of nembutal (Ross[1]) and amelioration of other symptoms of the toxemia synchronized the reduction of the blood pressure.

The satisfactory results obtained from the use of nembutal by the above dosimetric plan have convinced us that the procedure is rational and worthy of recommendation.

SUMMARY

1. High blood pressure (140 systolic or above) as the first clinical sign of toxemias of late pregnancy is presented.

2. High and rising blood pressure as indicative of an increasing and possibly a fatal pregnancy toxemia is discussed.

3. A dosimetric schedule for the use of nembutal based on the height of the blood pressure as a suggestive method of treatment is submitted.

4. The results of 60 cases of late pregnancy toxemias effectively treated with nembutal by the above scheme without the occurrence of convulsions, apoplexy, or death are reported.

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619 Florida Avenue

CLINICAL EXPERIENCES WITH ERGONOVINE

J. Irving Kushner, M.A., M.D., and Philip B. Wahrsinger, M.D.,
New York, N. Y.
(From the Obstetrical Service of The Bronx Hospital.)

THE chemistry of ergot has been the subject of many recent investigations and various alkaloids and amines have been described which possess biologic activity. In 1932 Moir[1] of London clearly demonstrated the presence of a hitherto unrecognized substance in ergot which showed prompt oxytocic action when orally administered and was found to be distinct from ergotoxine and ergotamine. This was substantiated by Dale.[2] Working independently, Davis, Adair, Rogers, Kharasch and Legault[3] of the University of Chicago isolated an active principle of ergot which they called "ergotocin."

Shortly after the appearance of this paper by Davis and his associates, Dudley and Moir[4] reported the crystallization of their product which was named "ergometrine." At the same time working in Baltimore, Thompson[5] isolated another principle which he called "ergostetrine." Finally Stoll and Burkhardt isolated "ergobasine." From the present available evidence it appears that ergotocin, ergostetrine, ergometrine, and ergobasine are the same. In fact all the investigators, each of whom independently discovered this new alkaloid of ergot, after investigation, acknowledged that the active principles each had isolated were identical.[6] In view of this, the Council on Pharmacy and Chemistry of the American Medical Association in session March 14, 1936,[7] decided it necessary to coin the new nonproprietary and not therapeutically suggestive name for this ergot alkaloid, "ergonovine." Meanwhile the various pharmaceutical houses had already capitalized the new findings: Lilly in the form of ergotrate; Wyeth in the form of ergoklonin; Burroughs and

Wellcome in the form of ergometrine; and Sandoz in the form of basergin.*

Davis, Adair and Pearl[8] using ergonovine malleate (ergotrate, Lilly) concluded that their cases exhibited an increased rate of involution and a lessened morbidity. Beecham[9] using ergostetrine (ergoklonin, Wyeth) also found an absence of subinvolution. DerBrucke[10] using ergostetrine (ergoklonin, Wyeth) found a too tonic action of this oxytocic giving sapremic temperatures.

PROCEDURE

As control cases 50 patients received no oxytocic medication during their stay in the hospital. The height of the fundus was measured daily as an indication of the involution of the uterus and a note was made as to the amount of bleeding and subjective symptoms of the patient. The next 400 consecutive deliveries were divided into groups of 100. The patients in each group were given one of the following medications immediately after the delivery of the placenta: (a) ergotrate (Lilly) 0.2 mg. intravenously (Kharasch and Legault's ergotocin); (b) ergoklonin (Wyeth) 0.2 mg. intramuscularly (Thompson's ergostetrine); (c) ergometrine (Burroughs and Wellcome) (Dudley & Moir's ergometrine) 0.125 mg. intravenously 50 cases and 50 cases 0.5 mg. intramuscularly; and (d) basergin (Stoll's ergobasine) 0.2 mg. intravenously. Again a daily note was made regarding the involution, morbidity and the subjective symptoms of the patients.

RESULTS

Involution.—The criteria of involutional progress are the extent of the recession of the uterus; the general consistency of its musculature and the character and amount of the lochia.

In the control group (Fig. 1) it can be seen that the uterus is always palpable above the symphysis at the tenth post-partum day and that its height averages 7 cm. above this level.

The group of cases that received ergonovine in the form of ergotrate (Lilly) showed the most rapid decrease in the size of the uterus as compared with the control cases as well as the cases receiving other medications. This increased rate of involution was most apparent during the last few days of the hospital stay.

The next most rapid decrease was seen in the patients receiving ergoklonin (Wyeth). Another factor must be considered here. The uterus in a patient after exhibition of ergotrate, intravenously, almost immediately became very firm and hard and remained so throughout the puerperium. This did not happen in any of the other groups of patients. For the treatment of post-partum hemorrhage due to atony of the uterus, from our experiences, ergotrate is to be recommended for its immediate results in causing the contraction of boggy uterus and keeping it in this condition.

With the other preparations it was often found necessary because of subinvolution or slow action to exhibit some other drug such as pituitrin or ergotrate either immediately or sometime during the hospital stay. The least desirable preparation from this point of view was ergometrine (Burroughs and Wellcome). Here, in 80 per cent of the cases it was necessary to use some other oxytocic. In the series of cases with basergin this was not as marked, although in 62 per cent of the cases it was found necessary to use ergotrate in order to prevent a subinvoluted boggy uterus.

*We are indebted to Lilly & Co. for the supply of ergotrate; to John Wyeth & Bro. for the ergoklonin, to Burroughs and Wellcome for the ergometrine, and to Sandoz for the basergin.

Ergoklonin while somewhat slower in action and therefore unsuitable for post-partum hemorrhage yet gave a fairly firm involuted uterus in about six to eight minutes after injection.

Bleeding.—A striking difference in the character of the lochia was noted on the discharge examination on the tenth post-partum day. The best results were obtained with ergotrate since 90 per cent of that group had no sanguineous discharge. In the control cases only 30 per cent were entirely free of bleeding. In the groups using ergometrine and basergin the percentage was the same as that in the control cases.

Morbidity.—A patient was considered morbid when her temperature reached 100.4° F. any two times after the first day post partum. These figures are corrected and constitute all temperatures of an obstetric nature that appeared in these 450 cases. The morbidity was highest (25 per cent) in the patients who received ergometrine and lowest (2 per cent) in the patients who received ergotrate; the ergoklonin series differed only slightly (4 per cent) from the ergotrate. In the patients receiving basergin the morbidity was 18 per cent.

Subjective Symptoms.—With ergoklonin, over 65 per cent of the women had pain, varying in intensity from mild to severe and limited to the first six days of the puerperium. In the ergotrate group this pain was experienced in only 12 per cent of the patients; while in the patients receiving ergometrine and basergin there was no pain. This would seem to imply perhaps a too tonically contracted uterus with the powerful ergotrate or ergoklonin.

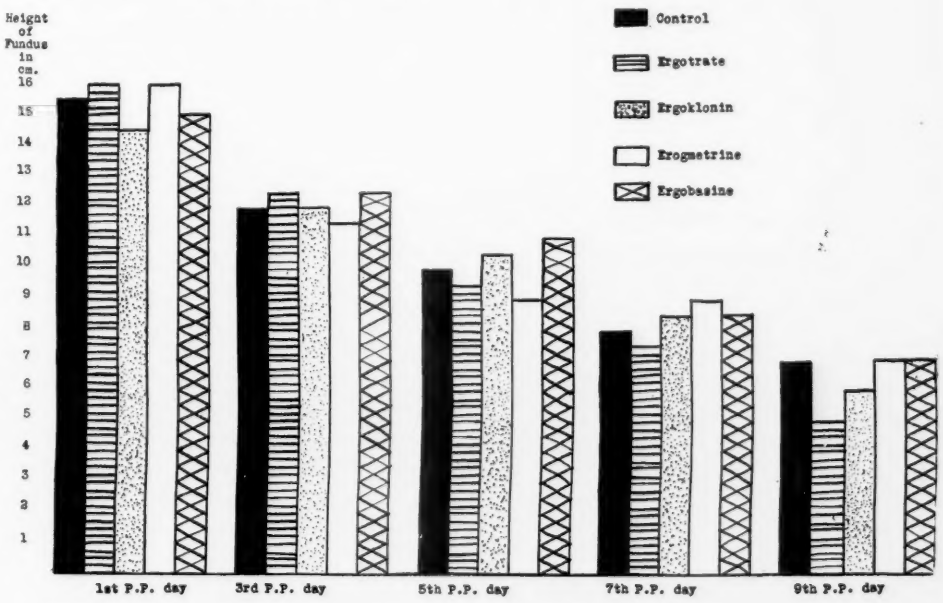

Fig. 1.—Height of fundus in centimeters above symphysis post partum, graphically shown after administration of various oxytocics.

DISCUSSION

The administration of ergoklonin gives all that can be desired in rapidity of involution, yet the annoying symptom of pain in 65 per cent of the women must be considered.

In this series ergometrine and basergin are shown to be of least value because of their unreliability in contracting the uterus. It is in these groups also that we find the greatest morbidity.

Ergotrate is considered to be the drug of choice. In this group there was immediate contraction of the uterus, the lowest morbidity, the smallest number of patients complaining of pain and the most sustained firm contraction of the uterus.

CONCLUSION

Because of the degree of involution of the post-partum uterus; the control of bleeding; the resulting firmness of the uterus and the lessened morbidity, ergonovine in the form of ergonovine malleate (ergotrate, Lilly) one ampoule (0.2 mg.) should be given intravenously immediately after the birth of the placenta. In the post-partum hemorrhage, due to atony of the uterus, this should be given before packing is instituted. Often it will be found that packing is not necessary.

In cases of subinvolution ergotrate will be found of value.

We are indebted to Dr. Meyer Rosensohn for his stimulation, kindly interest, and helpful suggestions in the preparation of this paper. Drs. J. Weisberg, M. Miller, and J. Alkoff, erstwhile residents on the obstetric division, aided in compilation of the figures.

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215 East Gunhill Road

1229 Clay Avenue

Bauer and Meller: Hemophilia in Women, Wien. klin. Wchnschr. 50: 495, 1937.

The authors answer in the negative the question whether the hereditary rule, now generally accepted, applies to all cases of hemophilia. They think that there are families in which the hemophilic factor becomes manifest only in males, that occasionally there are families in which the men and the women show hemophilic symptoms, and that in rare instances only the women exhibit the symptoms. The time is not yet ripe for the formulation of definite laws of the hereditary transmission of hemophilia. To be sure, severe and fatal hemorrhages as frequently occur in hemophilic men are only rarely observed in women. They describe four women whose disorder was characterized by a symptomatology similar to that of hemophilia as well as by a weakness of the thrombocytic apparatus. A combination of hemophilia and thrombopenia may occur and it is not justified to draw sharp distinctions between these two disorders. It may be assumed that the female sex organs provide a specific protection against fatal hemorrhages.

J. P. Greenhill.

CHORIOEPITHELIOMA OF THE FALLOPIAN TUBE

T. J. WILLIAMS, M.D., UNIVERSITY, VA.

(From the Department of Obstetrics and Gynecology, University of Virginia)

MARCHAND[1] in 1895 recorded the first instance of a chorioepithelioma of the Fallopian tube. Nurmberger[2] in 1932 stated that 33 authentic cases had been reported through 1930. He, however, did not include the case of Hartz[3] which he considered questionable, and the case of Moore,[4] both of which may be classified as tubal chorioepitheliomata. Since that time six additional cases have been reported by Stein,[5] Fleurent and others,[6] Savignoni,[7] Grudzew and Russky,[8] Bunnag and Bachman,[9] and Bianchi and Arrillaga,[10] making a total of 41 recorded cases. To this number we wish to add the following case:

CASE REPORT

Mrs. E. N. (No. 97777), aged twenty-three years, was admitted to the University of Virginia Hospital on June 14, 1932, complaining of a bloody vaginal discharge of six months' duration and a sharp pain in the right lower abdominal quadrant of three weeks' duration. The patient had been married for three years and had one child born in December, 1930, eighteen months previous to admission. The baby was nursed for three months and weaned in March, 1931. The menstrual periods recurred in June, 1931, three months after weaning, after which they recurred at regular monthly intervals with an average duration of seven days until December, 1931. The December period began at the usual time, but continued as a bloody vaginal spotting from that time until admission to the hospital in June, 1932.

The abdominal pain began first in February, 1932, in the right lower quadrant, at first quite acute and subsequently gradually subsiding. Three weeks before admission the pain recurred with sufficient severity to require confinement to bed, and was said to be associated with nausea, vomiting, chills, and fever. The appendix had been removed seven years previously.

At the time of admission the blood pressure was 115/65, temperature 98.8° F., hemoglobin 75 per cent Dare, red blood cells 4,585,000, white blood cells 4,036, and blood Wassermann negative. The examination revealed some generalized abdominal tenderness, although it was more marked in the right lower quadrant. An old scar of the appendectomy was present. The cervix was slightly patulous and showed small transverse lacerations. The body of the uterus was anterior, about normal size, somewhat limited in mobility with pelvic sensitiveness on attempts at movement. Nothing was palpated in the left adnexal region, while to the right of the uterus a soft, cystic, tender, fixed mass the size of an orange was outlined. There was moderately profuse uterine bleeding at the time of the vaginal examination.

The diagnosis seemed to hinge between an ovarian cyst, possibly intraligamentary, an old ectopic pregnancy, or a tuboovarian abscess.

June 18, 1932. *Operation:* Dilatation and curettage were done but no tissue was obtained. Exploration of the pelvis through an abdominal incision showed a mass the size of an orange in the right adnexal region, adherent to the omentum and intestines. After the separation of the adhesions the mass was found to be composed of the right tube and ovary, on the superior surface of which was an area about 5 by 7 cm., composed of dark brown degenerative tissue which suggested an old blood

clot. The uterus was of normal size and the left tube and ovary appeared normal. The right tube and ovary were removed.

Pathologic Report: (No. 102100.) (Dr. James R. Cash.) Specimen consisted of the right tube and ovary, which formed a mass weighing 55 gm., adherent to which was a mass of beef red-appearing tissue, which seemed to be bulging from the lumen of the tube.

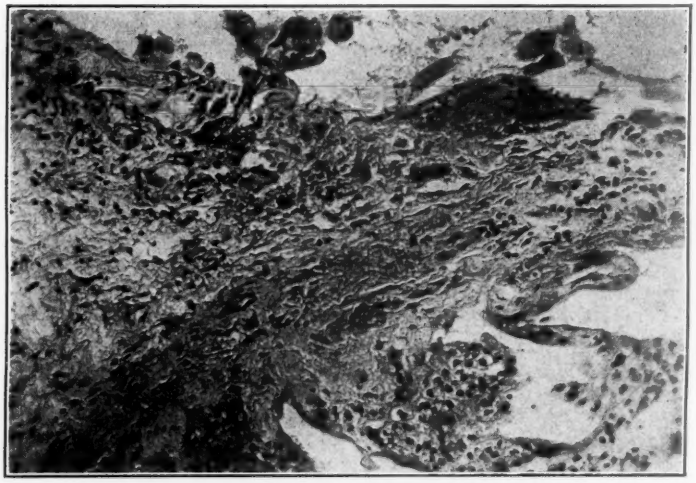

Fig. 1.—(×200.) Section near fimbriated end of tube showing chorioepithelioma lining the lumen and invading the wall of the tube.

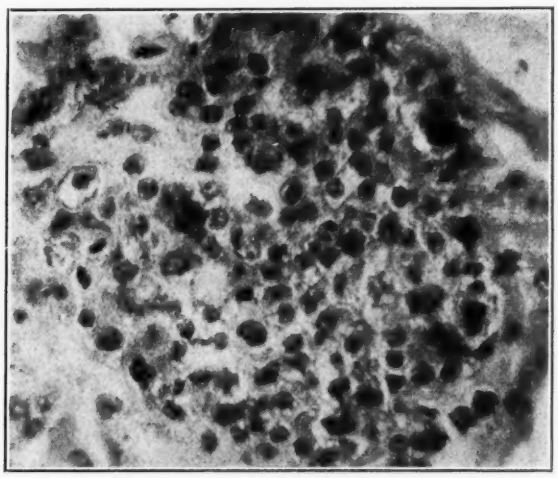

Fig. 2.—(×390.) Higher power of tumor showing group of Langhans' cells surrounded by syncytium.

Microscopic Examination.—In the ovary there were numerous small Graafian follicle cysts, which contained pink-staining coagulated fluid. The stroma of the ovary was very fibrous and edematous, and lightly infiltrated with lymphocytes. There were numerous old scars of corpora albicantia, some of which showed pigmentation with iron. Closely bound to the ovary by dense granulation tissue was the Fallopian tube, the wall of which was considerably thickened and heavily in-

filtrated by lymphocytes, mononuclears, and an occasional plasma cell. Arising from the wall of the tube was a large mass of partially calcified, very old granulation tissue, heavily infiltrated with lymphocytes filled with hemosiderin. Also arising from the distorted wall of the tube was a rapidly growing tumor composed of branching anastomosing cords of syncytium, partially surrounding small nests of more deeply staining Langhans' cells. These cells invaded the wall of the tube extensively, masses of tumor cells being intermingled with masses of degenerating smooth muscle and remains of rugae. A large portion of the tube was necrotic and very hemorrhagic.

Diagnosis: Chorioepithelioma of Fallopian tube. The immediate postoperative convalescence was uneventful. June 24, 1932: Friedmann's test, positive. June 30, 1932: Friedmann's test, positive. An x-ray of the chest was reported as negative for metastatic malignancy. Total hysterectomy with left salpingo-oophorectomy and radiation therapy over the pelvis was advised, but the patient refused any further procedures at the time and left the hospital, but promised to return.

July 22, 1932. The patient was readmitted to the hospital. She had been feeling well since leaving the hospital, and there had been no recurrence of the pain or bleeding. Vaginal examination showed the body of the uterus anterior, perhaps slightly enlarged, and pulled toward the right side. There was a definite induration to the right and posterior to the uterus. Nothing abnormal was felt in the left adnexa. Friedmann's, strongly positive. An x-ray of the chest was reported as negative for metastatic malignancy.

July 26, 1932. Operation: Exploration of the pelvis showed the uterus small and movable. The left ovary contained a cyst the size of a lemon. The ileum was adherent to the right broad ligament where adhesions had been separated at the time of the previous operation. Total hysterectomy and left salpingo-oophorectomy were done.

The postoperative convalescence was complicated by separation of the abdominal incision and extrusion of the intestines on the ninth postoperative day. Secondary closure was done and was followed by an uneventful convalescence.

Pathologic Report (Dr. James R. Cash): Specimen consisted of uterus, left tube, and left ovary, with a combined weight of 110 gm. The uterus and endometrium appeared grossly normal. The ovary contained a hemorrhagic cyst 6 by 4½ by 5 cm., which on section appeared multilocular and contained a yellowish thin serous fluid. The tube appeared normal.

On microscopic examination the sections of the uterus and tube appeared normal. The endometrium seemed premenstrual in character. The wall of the cyst of the ovary was composed of fibrous ovarian stroma, and was lined by layers of large polyhedral cells resembling lutein cells.

Diagnosis: Normal uterus and tube, lutein cell cyst of ovary.

August 17, 1932. Friedmann's, strongly positive.

The patient refused x-ray therapy on this admission and left the hospital on Aug. 17, 1932.

October 21, 1932. The patient reentered the hospital. Since the previous admission she had been feeling well, had no complaints, and was gaining weight. Vaginal examination revealed the vagina and pelvis to be free of any nodules or masses. An x-ray of the chest was negative for metastatic malignancy. Friedmann's, strongly positive. October 25 to 29, 1932. X-ray therapy (200 K. V., ½ mm. copper and 1 mm. aluminum), 1,890 r. units given to the pelvis through three portals and 270 r. units given over posterior chest. She was discharged from the hospital on Nov. 1, 1932.

December 12, 1932. Weight 100 pounds; felt well. The pelvis and vagina were free of masses and nodules. Friedmann's, negative.

May 22, 1933. A letter received from the patient stated that she was feeling well; weight 117 pounds.

Sept. 13, 1933. The patient had no symptoms. An x-ray of the chest was reported as suspicious of metastatic malignancy, but not pathognomonic. Friedmann's, positive. No masses or nodules were present in the pelvis or vagina. A neurologic examination and an examination of the eye grounds revealed normal findings. Sept. 19 to 22, 1933. X-ray therapy, 1890 r. given over pelvis, and 1,260 r. given over chest.

Jan. 1, 1934. Friedmann's, positive. An x-ray of the chest reported as suspicious for metastatic malignancy but not pathognomonic. X-rays of the skull and the pelvic bones were negative for metastases. The visual fields and eye grounds were normal. General physical examination was normal. The pelvis and vagina were free of masses and nodules. Jan. 5 to 14, 1932. X-ray therapy, 1,890 r. given to the pelvis and 2,500 r. to the chest through two anterior and two posterior portals.

March 15, 1934. Friedmann's, strongly positive. The pelvis was free except for some fullness rather high on the left side of the pelvis. X-ray of the chest showed findings which were consistent with metastatic malignancy. The eye grounds were clear. March 19 to 30, 1934. X-ray therapy, 5,000 r. units given over the chest through four portals. March 30, 1934. An x-ray of the chest showed the findings to be less marked and not as suggestive of metastatic malignancy as at the time of the previous examination two weeks ago.

April 9, 1934. A letter was received, which stated that the patient was paralyzed on the right side.

April 28, 1934. Patient died at home, apparently from brain metastases one year and ten months after the original operation and diagnosis. No postmortem examination was obtained.

NOTE: The patient lived about 250 miles from the Hospital and was practically indigent, and in the early days of her illness rather uncooperative, which accounts for the delay in completing the treatment in the early stages of the disease, and for the prolonged periods of absence during the follow-up procedures.

DISCUSSION

Extrauterine chorioepithelioma may originate either as a primary growth following an extrauterine pregnancy, or as a so-called ectopic chorioepithelioma, the villi having been transported during and subsequent to a previous uterine pregnancy, without initial malignant tumor formation in the uterus. It may of course be metastatic, from a primary malignant growth in the uterus, or teratogenous in which the tumor arises from chorionic cells included in a teratoma. To these generally accepted modes of origin of extrauterine chorioepithelioma, Hamdi[11] has recently suggested the possibility of its histogenesis from rudimentary rests, or by metaplasia.

The metastatic chorioepitheliomata secondary to a primary growth in the uterus are ordinarily not included in the discussions of primary chorioepithelioma of the Fallopian tube. Those of teratogenous origin most commonly arise in the ovary, teratomata usually forming the point of origin of chorioepitheliomata of the ovary and the subsequent metastatic lesions in individuals in whom no pregnancies have occurred. The majority of instances of tubal chorioepithelioma are of the primary type, arising in the tube subsequent to a tubal pregnancy. In support of this contention, Meyer[12] has pointed out the occurrence of hydatidiform degeneration of chorionic villi in instances of tubal gestation.

The ectopic type of chorioepithelioma of the tube, in which the villi have been transported, subsequent to a previous intrauterine pregnancy, without a primary tu-

mor in the uterus, is unusual. Fleurent, Keller and Meyer[6] have pointed out that there are no instances of ectopic tubal chorioepitheliomata with certainty. Naturally in tubal chorioepithelioma it is often quite difficult to disprove the occurrence of an early tubal pregnancy, which might have been the origin. While it is impossible to prove that chorioepithelioma of the tube or ovary is of the ectopic type, on the other hand the possibility of its occurrence is shown by instances of chorioepithelioma of the broad ligament without demonstrable evidence of chorioepithelioma elsewhere, unless one assumes that the original uterine growth had spontaneously disappeared. One such patient was under our care, in whom several months after an abortion, a pelvic mass was found. A curettage of the uterus was done and no tissue was obtained which suggested chorionic cells. Examination of the uterus, tubes, and ovaries through an abdominal incision revealed entirely normal structures to inspection and palpation. The mass in the pelvis was an inoperable hemorrhagic tumor of the right broad ligament. While at that time the diagnosis was not confirmed either by biopsy or the Aschheim-Zondek test, the patient developed pulmonary metastases and died about two months after the exploratory operation, in spite of radiation therapy. Unfortunately no postmortem examination was done, and it is possible that a small focus of malignant chorionic cells existed in the uterus, although on curettage and on gross examination of the pelvic structures there was no evidence of tumor growth or nodules. Assuming that the diagnosis of chorioepithelioma was justified, and with the absence of any demonstrable tumor in the uterus, this would have to be considered as an instance of ectopic chorioepithelioma due to the transportation of villi during and subsequent to the abortion some months previously.

In our present case the tumor may have been primary, following an early tubal gestation or ectopic from transported villi during and subsequent to the pregnancy eighteen months previous to the first admission to the hospital. It most likely followed an early tubal pregnancy which probably occurred in December at the time the vaginal bleeding began, and which was very likely partially aborted from the tube in February at the time of the severe abdominal pain, which gradually subsided. The recurrence of the severe pain three months later (three weeks before admission to the hospital) was associated with the growth, invasion, and extrusion of the malignant chorionic cells at the fimbriated extremity of the tube.

The life cycle of a tubal chorioepithelioma is usually considered as divisible into three periods: first, that of the extrauterine pregnancy, second, a latent period, and third, the period of tumor growth. Assuming our case was one following an extrauterine pregnancy, it may be easily divided into these three periods, the period of extrauterine pregnancy from December, 1931, to February, 1932, the latent period from February to May, and the period of tumor growth from May onward.

The findings on the Friedmann test are of interest in our patient, as after numerous positive tests it became temporarily negative, following the complete operation and pelvic and abdominal radiation. It was found positive again nine months later and remained positive until death in spite of extensive radiation therapy. The pregnancy urine test is of great value in the diagnosis and prognosis of chorionic tumors. For a period of several months the only evidence that a cure had not been effected in our patient was the presence of a positive Friedmann's test. The single negative finding stimulated an optimistic outlook for her future, which proved to be false and led to a sense of security which was not justified.

Of the cases reported in the literature possibly three patients may have recovered from the disease. The patient of Albert[13] was well one year at the time of the report. Lofquist's[14] case is recorded as a recovery and Miles Phillips'[15] patient had survived for something over two years. Assuming that these instances may be considered as recoveries, it gives a mortality of about 93 per cent. In general, however,

chorioepithelioma of the Fallopian tube may be considered as a fatal disease, as there may be considerable question concerning the permanence of the recovery in the recorded cases. As exemplified by our patient, the mere survival without symptoms for a year or so does not necessarily mean recovery.

SUMMARY

An instance of chorioepithelioma of the Fallopian tube, which was treated by operation and radiation, is reported. This seems to be the forty-second case to be recorded in the literature.

The modes of origin of extrauterine chorioepitheliomata are discussed, and it is believed that in our patient it developed primarily in the tube subsequent to a tubal pregnancy.

The value of tests for the luteinizing hormone in the urine in cases of chorionic tumors is shown. A persistent positive reaction even in the absence of all signs and symptoms seems to indicate a serious prognosis, while too much reliance should not be placed in a single negative test.

The mortality in the reported cases has been about 93 per cent.

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THE MANAGEMENT OF PREGNANCY AND LABOR COMPLICATED BY TRIPLETS*

John C. Hirst, A.B., M.D., Philadelphia, Pa.

(From the Preston Retreat)

THIS record of a triplet pregnancy is presented not as a "case report," but as instructive experience derived from unusual behavior, study, and management of a potentially dangerous condition. A review of the fate of triplets (all unreported) in three institutions attended by the author discloses interesting facts. In the Philadelphia Lying-in Hospital from 16,857 births of over twenty weeks' gestation two sets of triplets have occurred.

The first patient, para ii, delivered at thirty-one weeks: A, male, O. R. A., 4 pounds 1½ ounces; B, male, occ. post., 1 pound 12 ounces; C, female, footling, 3 pounds 10 ounces; pregnancy was featured by weight increase in the last four months from 126¼ to 162 pounds, and by maximum blood pressure of 156/94; labor was

*Read at a regular meeting of the Philadelphia Obstetrical Society, May 6, 1937.

rapid, first and second stages only three hours thirty-seven minutes, third stage fifty-seven minutes; delivery was simple; puerperium uncomplicated; infants all survived (Dr. Robert A. Kimbrough). The second patient, para iii, delivered "under thirty weeks": A, male, O. L. A., 2 pounds 12 ounces; B, male, O. L. A., 2 pounds 14 ounces; C, male, "version," 2 pounds 8 ounces; pregnancy uneventful, patient recalcitrant; labor slow, first stage nine hours, second stage two hours fifty-five minutes, third stage uncomplicated; delivery satisfactory; recovery normal; infants all died from prematurity.

In the Hospital of the University of Pennsylvania the last 15,000 viable deliveries produced 1 set of triplets from a para i, aged twenty-six, who was delivered at thirty-one weeks of one female and two male infants, the first by outlet forceps; pregnancy normal; labor vague, "several days," delivered 7.75 hours after rupture of membranes "without contractions," forty-five minutes between infants, third stage ten minutes; puerperium complicated by prolonged morbidity (endometritis); infants, 1 stillborn, 1 died on the fifth day, and the third unknown.

In the Preston Retreat, among 16,500 pregnancy registrations beyond twelve weeks of gestation there has appeared but one set of triplets. The record of this case is briefly summarized below to illustrate the following features: (1) New prenatal plan in supporting multiple pregnancy; (2) prolongation of triplet pregnancy to the thirty-eighth week of gestation; (3) marked bilateral hydronephrosis due to large pregnancy, resulting in: (4) distorted phenolsulphonephthalein and indigocarmine urinary functional tests; (5) no proportional increase in quantitative estrogenic substance and anterior pituitary-like urinary hormone analysis; (6) abruptio placentae between births of second and third infants; (7) unusually fine and large triplets.

Oct. 3, 1936: Mrs. M. K., aged twenty, married to a slight man of twenty-one years, stated that no multiple pregnancy had occurred in either immediate family. The mother had carried and spontaneously delivered one living child without any complication, registering with this second pregnancy in good condition on the above date; due for confinement March 21, 1937.

General physical examination disclosed a well-developed young woman, height 5 feet 3 inches, with normal heart and lungs. The obstetric examination was also favorable, the only features as of October 3 being slight edema of the right leg, moderately relaxed birth canal, and average gynecoid pelvis.

Until February 1, the prenatal progress was subjectively and objectively good, although cervical cauterization, treatment for secondary anemia (hemoglobin 65 per cent—Dare), dental attention and anodyne for left abdominal parietal neuralgia were administered. On February 1, at thirty-third week of gestation, the patient was admitted to the hospital ward on account of excess weight gain (see), and severe persistent bilateral ankle edema, for fluid control, rest, restricted salt ingestion, mild catharsis, urea diuresis, and high mineral-vitamin diet including extra beef, milk, eggs, dicalcium-phosphate with viosterol, and capsules of vitamins A, B, D, and G. The urine remained virtually negative, showing only a faint trace of albumin in one out of twelve examinations, and no other abnormality, although the sp. gr. averaged

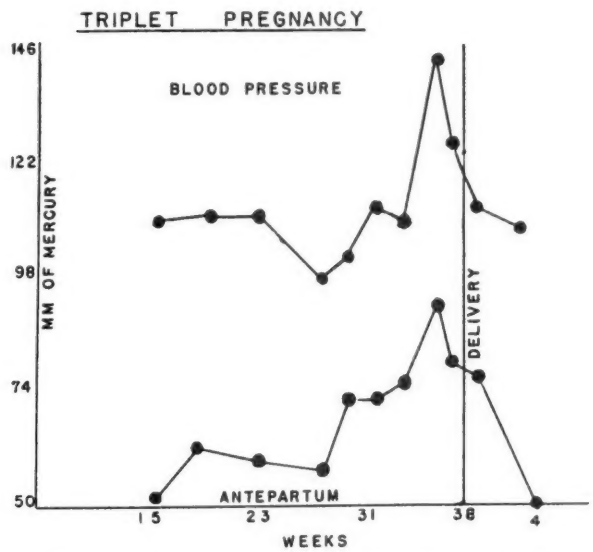

Fig. 1.—Moderate hypertension at thirty-sixth week.

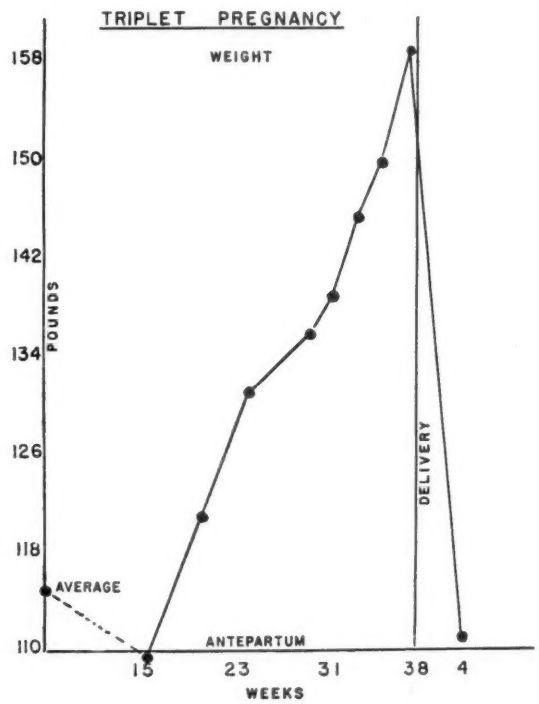

Fig. 2.—Rapid weight increase with general edema in spite of fluid balance efforts.

only 1.014. Directly after admission, a positive twin, possible triplet diagnosis was made; the latter was confirmed by x-ray film, yet never were more than two fetal heart sounds audible, the greatest variation being 9 beats per minute.

On March 4, one amniotic sac ruptured spontaneously at 4:00 A.M., and labor began fifteen minutes later, progressing very actively to second stage at 7:15 A.M. The infants were delivered at 8:12 A.M., 8:23 A.M., and 8:31 A.M., each, after arti-

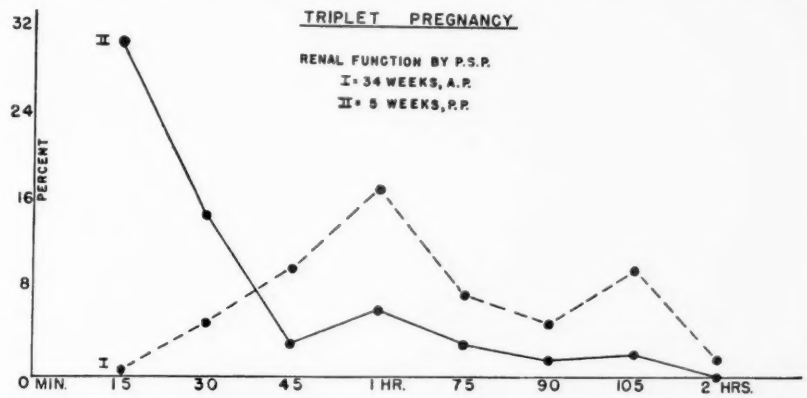

Fig. 3.—Ascending "hydronephrotic" antepartum, and normal steep descending postpartum curve after intravenous phenolsulphonephthalein injection.

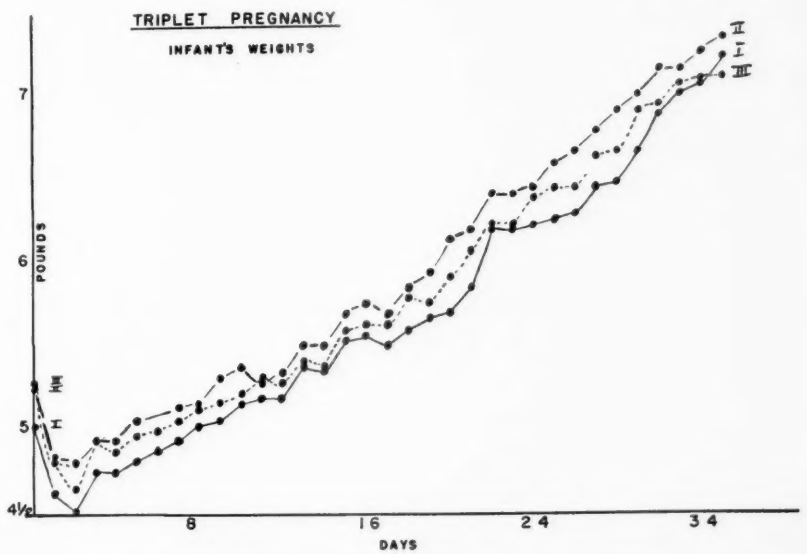

Fig. 4.—Amazingly vigorous identical female infants. Placenta, monochorionic (monozygotic).

ficial rupture of the second and third amniotic sacs, by easy manual rotation from O. R. P., O. R. P., and O. L. P., followed by low Tucker-McLane forceps extraction without injury. However, sharp bleeding with the birth of the third infant, followed by immediate descent of the placenta to the introitus and simple expression in Schultze mechanism indicated complete abruptio placentae during the last delivery.

The placenta proved to be monochorionic or uniovular, weighed 1,364 gm. and measured 22 by 24 by 4 cm. The infants were identical females, all amazingly healthy and vigorous, weighing 2,286, 2,409, and 2,427 gm., respectively. Last heard from, they were thriving perfectly at six months of age, continuing on acidified evaporated milk, dextrimaltose, and soluble irradiated ergosterol.

The puerperium was abnormal chiefly from severe secondary anemia requiring two transfusions, plus slight sapremic morbidity associated with lochiometra. Twenty-seven days after delivery a second cystoscopic investigation was completed, which showed no bladder or ureteral orifice pathology, and only slight hydronephrosis of the right ureter, a striking contrast to the prior examination two days before birth, when there was great edema and congestion of the trigone, very high and divergent ureteral orifices and bilateral extreme nonobstructive hydronephrosis (see Table II). The mother's condition on discharge was excellent. There was only 2 fingers' diastasis of the recti abdominis muscles and no renal ptosis. The lochia had ceased, the uterus had involuted in good position to 3 fingers above the symphysis pubis, while the remainder of the birth tract was exactly as before.

TABLE I. ABDOMINAL MEASUREMENT BEFORE AND AFTER DELIVERY

HEIGHT—61¼ IN. OR 155.6 CM.		
	37TH WEEK A.P.	5TH WEEK P.P.
Circumference at umbilicus	42 in.—106.7 cm.	29 in.—73.7 cm.
Symphysis to ensiform	22 in.— 55.9 cm.	9 in.—22.9 cm.

TABLE II. CYSTOSCOPY

		37TH WEEK A.P.	5TH WEEK P.P.
Retention	Right	79 c.c.	11 c.c.
	Left	96 c.c.	None
Injection	Right	Not done	31 c.c. (Recovered)
	Left	Not done	7 c.c. (Recovered)
Function (Indigo-carmine)	Right	23 Min.-(Light)	7 Min. (Dark)
	Left	19 Min.-(Light)	7¼ Min. (Dark)
Microscopy	Right	Occ. W.B.C.; 3-5 R.B.C. many bac.; many gram (−) rods.	Few pus cells. Mod. squamous. Mod. gram + cocci No T.B.
	Left	Occ. R.B.C. and mucus; many bac. Many gram (−) rods; occ. gram + cocci (Hem. staph.)	Not done

TABLE III. TWENTY-FOUR-HOUR URINARY HORMONE ASSAY. QUANTITATIVE VALUES AT THIRTY-SIXTH WEEK MODERATELY INCREASED, BUT NOT IN PROPORTION TO PLACENTAL MASS

Estrin:	Active, 2,000 Rat units Combined, 4,000 Rat units (Active plus inactive)
Prolan B:	3,200 Rat units

CONCLUSIONS

1. It is possible to carry triplet pregnancy close to maturity and to secure vigorous infants.

2. Hospital study and control from at least thirty-four weeks' gestation is necessary, including rest, high protein-mineral-vitamin, and low salt-water diet.

3. Hydronephrosis of multiple pregnancy in the last trimester precludes accurate urinary excretion renal function tests, and possibly interferes with quantitative twenty-four-hour urinary hormone valuation. Further analyses of hormone content in urine and placental substance from multiple pregnancies will be helpful in determining their source values.

4. Premature separation of a normally situated and conditioned placenta must be considered in late triplet pregnancies.

HYPERPLASIA IN THE EPITHELIUM OF THE UTERINE TUBES

EDGAR ALLEN, M.D., NEW HAVEN, CONN.
(From the Department of Anatomy, Yale University School of Medicine)

I HAVE frequently sought for mitotic figures in the epithelium of the uterine tubes, after having been greatly impressed by the rapid growth of the vagina and uterus in response to the ovarian follicular hormone. Periods of retrogression occur paralleling the menstrual period in primates (Snyder, 1924; Allen, 1928) and the diestrus period in lower mammals (Allen, 1922; Snyder, 1923). These degenerative phases alternate with periods of repair and regeneration. Nevertheless, search for mitoses in the tubal epithelium has been very disappointing even though the vagina and uterus of the same animal may be growing rapidly.

With the use of the drug colchicine for the study of hyperplasia, it has been possible to hold dividing cells in metaphase, thus accumulating all cells dividing in a period of from ten to twenty hours (Allen, Smith and Gardner, 1936-1937). In this condition they are easily recognizable, making the count of mitoses for a mitotic index extremely convincing. While previously 10 to 20 mitotic figures per section might be considered an index of hyperplasia, with the colchicine method several hundred or even over a thousand may occur in a single cross-section of the vaginal epithelium of the mouse.

This new method has emphasized the epithelial hyperplasia in the uterine tubes of the mouse, rat, and monkey. Cell divisions are most numerous in the tubes of the normal animal when large follicles are

present in the ovary. The ovariectomized animal injected with ovarian follicular hormone shows that the growth characterizing the rest of the genital tract in response to this stimulation also extends up into the tubes. Growth is especially active in the fimbriated ends. It is difficult even with the colchicine method to find many mitoses in the uterine end of the tube. The illustrations show the high incidence of mitotic figures in the uterine tubes of the monkey. At least twelve mitotic

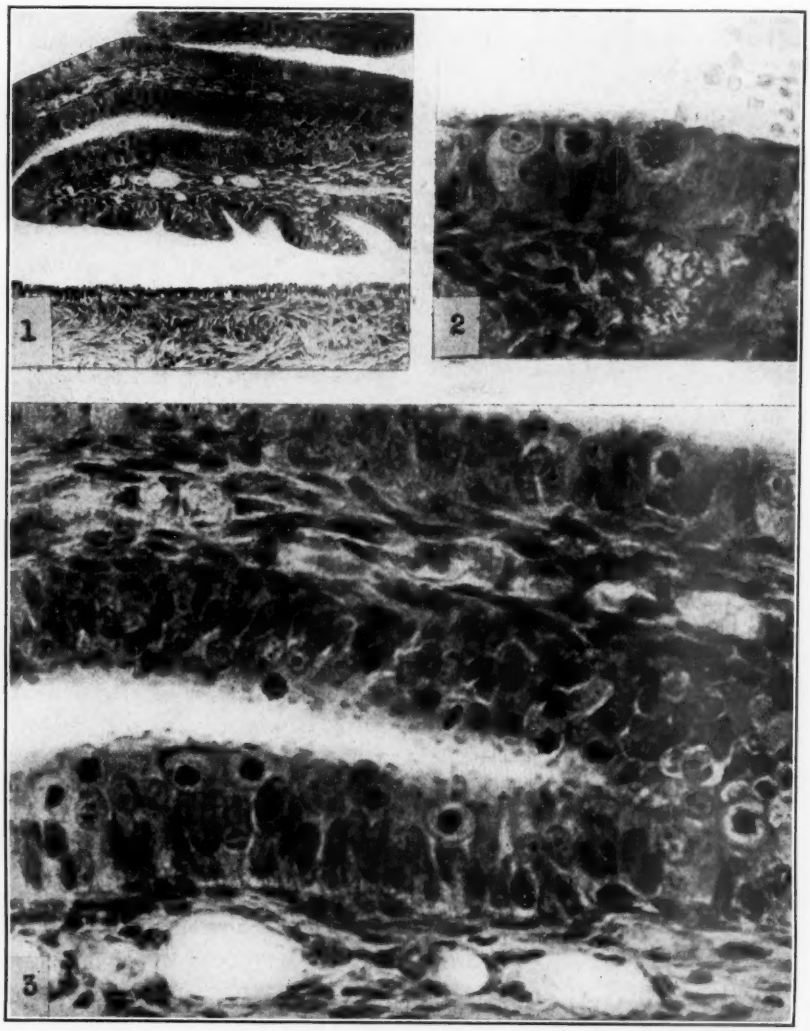

Fig. 1.—A portion of the fimbria of a uterine tube of a monkey. Many mitotic figures are found in the epithelium, being particularly numerous in localized areas. The germinal epithelium of the ovary seen in the lower part of the photomicrograph shows no mitotic activity.

Fig. 2.—A photomicrograph of a small portion of the tubal epithelium showing a polar view of a metaphase stage. Individual chromosomes may be recognized. The chromatin of a second dividing cell is clumped, as frequently occurs in cells influenced by colchicine.

Fig. 3.—Higher magnification of Fig. 1, above.

figures have been found in a single section of the fimbria adjacent to the germinal epithelium of the ovary (Fig. 1). Fig. 2 is a polar view of a metaphase stage showing the ends of individual chromosomes protruding from the mass, while at the left is a mitotic figure in which the chromosomes have been clumped, as frequently happens in cells influenced by this drug. Fig. 3 shows 10 mitotic figures in a restricted field. Polar and equatorial views can be noted and also several cells with the clumped chromatin.

SUMMARY

Waves of growth, especially evident in the epithelium, extend into the uterine tubes. They occur in normal animals when large follicles are present in the ovaries and are induced in ovariectomized animals by the follicular hormone. This is similar to, and coincident with, the hyperplasia in the vagina and uterus.

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TUBAL PREGNANCY

An Analysis of 445 Cases

P. Graffagnino, M.D., Louis Seyler, M.D., and
Moss M. Bannermann, M.B., New Orleans, La.

(From the Department of Gynecology, Louisiana State University Medical Center, and the Gynecological Services of New Orleans Charity Hospital)

THE tubal pregnancies which have occurred in the Charity Hospital in New Orleans have been reviewed several times in the past (Am. J. Obst. & Gynec., July and August, 1922). It is the purpose of this paper to bring the statistics up from the review of 1906 to 1920, by one of us, through 1936. In the files of the Charity Hospital Record Room there are 490 cases of ectopic pregnancy between the years 1919 and 1936. For this period, the total number of gynecologic admissions was 62,853, an incidence of 0.78 per cent of ectopic pregnancy. In this group of cases, 63 deaths occurred, a mortality rate of 12.8 per cent.

For the purpose of study only 445 records were available and this study is predicated on these records only. Of these 445, the earlier records are not as definite and complete as the more recent ones, and this explains some of the incomplete graphs and tables presented.

There were 220 white patients and 225 colored patients in this series of cases. The patients varied in age from seventeen years to forty-seven years.

In this group there occurred 51 deaths, 21 white patients and 30 colored patients, a mortality rate of 11.4 per cent. All age groups were affected proportionally to the age groupings of the entire series. The majority of the white cases occurred between the ages of 27 and 36 years, and the colored cases between the ages of 22 and 31 years in the entire series.

The greatest number of white patients were between the ages of 27 and 31 years while the colored patients were between the ages of 22 and 26 years, there being a five-year difference in the age groups. The white patients increase in number from 21 to 31 years, the colored patients start high at 22 and decrease in number to 32 years, just a reverse in the age groupings.

PREVIOUS INTRAUTERINE PREGNANCIES

There were 69 patients in this series who were nulliparous (15.5 per cent); 84 patients who had had one pregnancy (18.87 per cent); and so on, two patients having had 16 pregnancies.

The majority of the patients reported had never had a miscarriage (207 cases, or 46.51 per cent); 94 patients (21.12 per cent) had had one miscarriage; and on up to one patient, as seen reported, having had 10 previous miscarriages or abortions.

MENSTRUAL DISTURBANCES

The menstrual disturbances were quite variable. There were 78 patients (17.52 per cent) who gave a history of no irregularity of menstruation; 142 patients (31.91 per cent) who gave a history of one missed period; and 97 (21.8 per cent), two missed periods; and so on up to two patients who stated that they had not menstruated for eight months.

There were 45 patients (10.11 per cent) who gave a history of menorrhagia, and 30 patients (6.9 per cent) who gave a history of metrorrhagia.

TUBAL INVOLVEMENT

It is interesting to note how much more frequently the right tube is involved than the left in both the colored and the white races. This may be due to the frequency of appendicitis associated with perisalpingitis interfering with the normal physiologic peristaltic action of the tubal musculature. There is a slight torsion of the uterus to the right normally which may in some way also interfere with the peristaltic movements of the tube, thereby retarding progress of the impregnated ovum.

DURATION OF HOSPITALIZATION

The stay in the hospital in weeks was recorded, and it was found that the majority of the patients stayed over two weeks, the average stay being 18.6 days. There were, however, 36.4 per cent who left the hospital between seven and fourteen days. Almost all of the 8.26 per cent of patients recorded as staying less than a week died.

SYMPTOMS

The symptoms as presented by the patients on admission were varied, but those most frequently found were cramps or pains in the lower abdomen, bleeding, faint-

ing, weakness, nausea, and vomiting. A list of the presenting symptoms is appended with the number of patients recorded as having had them:

Pain:	CASES
Cramps in lower abdomen	123
Acute pain in abdomen	113
Pain in right side	50
Pain in left side	37
Pain in lower left quadrant	34
Pain in lower right quadrant	39
Pain in back	15
Pain	10
Pain about umbilicus	4
Pain in upper abdomen	3
Pain in shoulder	5
Labor pains	8
Headaches	3
Menstrual Disorders:	
Bleeding	149
Uterine cramps	4
Dysmenorrhea	2

Vasomotor Disturbances:	CASES
Fainting	39
Faintness	34
Weakness	34
Shock	9
Disorders of G. I. Tract:	
Diarrhea	9
Nausea	30
Vomiting	60
Constipation	3
Lump in abdomen	18
Swelling in abdomen	7
Tenesmus	11
Dysuria	9
Polyuria	1
Fever	4
Chills	2

DIAGNOSIS

The diagnoses on admission were as varied as the symptoms presented would suggest, but in spite of these variable symptoms, 276 cases were diagnosed as ectopic pregnancy (62.02 per cent). Of the patients who died, the admission diagnoses were similar to those of the entire series except that there was less accuracy, only 51 per cent being diagnosed correctly.

A list of the admitting diagnoses is presented not to shame those of us who made them but so that others may see where confusion might arise and better their own statistics:

	CASES
Ectopic pregnancy	276
Abortion	21
Chronic pelvic cellulitis	15
Bilateral salpingitis	11
Acute pelvic cellulitis	13
Cystic ovary	16
Fibroids	22
Pelvic abscess	6
Salpingo-oophoritis	12
Tuboovarian abscess	16
Acute appendicitis	11
Chronic salpingitis	9
Pyosalpinx	5
Subacute appendicitis	4

	CASES
Dermoid cyst	1
Left ovarian cyst	3
Acute indigestion	2
Endometritis	2
Cholelithiasis	1
Right salpingitis	1
Peritonitis	1
Typhoid fever	1
Intestinal obstruction	1
Ruptured uterus	1
Prolapsed uterus	1
Puerperal sepsis	1
Retroverted uterus	1

The operations performed on these patients are listed:

	CASES
Right salpingectomy	147
Left salpingectomy	78
Right salpingo-oophorectomy	94
Bilateral salpingectomy and right oophorectomy	8
Bilateral salpingectomy	8
Bilateral salpingo-oophorectomy	11
Bilateral salpingectomy and left oophorectomy	5
Hysterectomy	8

	CASES
Bilateral salpingo-oophorectomy and fundusectomy	1
Right oophorectomy, dilatation and curettage, trachelorrhaphy; perineorrhaphy	1
Salpingo-oophorectomy, Norris suspension, appendectomy	1
Salpingo-oophorectomy, appendectomy	2
Salpingo-oophorectomy, conization of cervix, removal of condyloma	1

Of the 8 hysterectomies done, 5 of the patients died, indicating definitely that major surgical procedures should not be done in the presence of ectopic pregnancy.

The transfusions given in the entire series are appended:

	CASES
None	287
One	86
Two	23
Three	6
Four	1
?	9
Autotransfusions	7

We feel hesitant about reporting the small number of transfusions which were given when we realize what a valuable therapeutic measure it is in this type of case. However, it must be appreciated that we are dealing with negro patients and with patients from all over the state of Louisiana, whose relatives are often difficult to contact for donors and when contacted are reluctant to give their blood. In the 51 patients that died, 9 transfusions were given preoperatively, and of these only 1 patient died before operation. The transfusions, however, were given immediately before operation or while the patient was on the operating table.

The sedimentation rate is known to be of definite and valuable aid in making a diagnosis of inflammation in the pelvis. On the few patients (12) who had a sedimentation rate recorded we found that in ectopic pregnancy it is not rapid as in acute infections, but remains prolonged, in our series averaging about forty-seven minutes.

This point bears out the contention of Dr. Paul Titus of Pittsburgh who makes the statement that in those patients with elevation of temperature and pulse rate with leucocytosis, the blood sedimentation test is of immeasurable value in helping one to make a differential diagnosis between ectopic pregnancy and acute inflammatory processes. It remains persistently prolonged within normal range.

ANESTHETIC

The anesthetics used on these patients were:

	CASES
Ethylene	100
Ether	214
Spinal	104
Local	5
Nitrous oxide	3
Epidural	4
None	1

Contrary to the general belief, ectopic pregnancy cases do as well under one form of anesthesia as another.

DEATHS

As stated before, there were 51 deaths in this series of cases. Twelve patients died before operation, 5 died on the operating table, and 34 died after operation.

Of the patients who died, 35.3 per cent were admitted in shock, 25.4 per cent in poor condition, 17.7 per cent in fair condition, and 21.4 per cent in good condition. The preoperative condition of the patients was analyzed: 24.8 per cent were operated upon in shock, 34.7 per cent in poor condition, 12.4 per cent in good condition, and 8.1 per cent in fair condition.

The preoperative medication in the patients who died was palliative in most instances, 27 cases (55 per cent); there were 10 patients (20 per cent) who received subcutaneous clyses; 5 patients (10 per cent) received intravenous infusion; 2 patients (4 per cent) received acacia with transfusions or infusions; and 7 patients (14 per cent) received blood transfusions.

The temperature of the patients who died was analyzed, and it can be seen that it ranged from 98 to 101° in the majority of cases, only a few patients showing a temperature as high as 104.

The lymphocyte count as recorded in some of the charts of the deaths ranged from 8,000 to 35,000 white blood cells.

1215 Union Building

IRREDUCIBLE, STRANGULATED, COMPLETE PROLAPSE OF THE UTERUS, COMPLICATED BY SLIDING HERNIA OF THE CECUM AND INTESTINAL OBSTRUCTION

ROBERT T. FRANK, M.D., NEW YORK, N. Y.
(From the Gynecological Service of the Mount Sinai Hospital)

ALTHOUGH complete prolapse of the uterus, often complicated by enterocele, is of frequent occurrence, loss of reducibility and consequent incarceration is most infrequent.

A search of the literature, including a study of the older textbooks published before the operative era, shows but one report of conditions such as were encountered in this patient.

v. Jaschke[1] in *Stoeckel's Handbuch der Gynäkologie* states that "ulceration, edema and perivaginal phlegmons may develop in a prolapse followed by purulent metro- and endometritis. The swelling may reach such a degree, the phlegmon may extend so rapidly to the rest of the cellular tissues that the prolapse, within a short time becomes irreducible." This author observed one case which spontaneously recovered through gangrene and sequestration of the major portion of the uterus. "In the majority of cases, however," he continues, "death results whether the patient is untreated, or an attempt to perform hysterectomy is made."

CASE REPORT

The patient was a 42-year-old, Irish housewife, para ii. Last pregnancy ten years ago. Prolapse of the uterus, always readily replaceable, existed for one year. For fourteen days preceding admission, the prolapse could not be reduced, confining the patient to bed. There was difficulty in micturition from the onset. No flatus or feces were expelled for the last two days.

She was admitted to the Gynecological Ward of Mount Sinai Hospital, the evening of Jan. 7, 1937. Temperature was 100.8° F., pulse 72, and blood pressure 100/80. The patient was thin, mental reactions were sluggish, and she was apparently not acutely ill. Abdomen was tympanitic and moderately distended. Inspection showed a huge mass protruding from and covering the vulva. The long diameter was 12 inches, transverse diameter 6 inches, and the circumference 19 inches. The mass was pine-apple-shaped, being wider at midsection than at its base. The apex was formed by the huge, ulcerated and edematous cervix, the surface consisted of the everted vaginal mucosa, dry, scaly, with "bursting" ulcers in several areas. The color was deeply cyanotic, the consistence boggy, the percussion note posteriorly tympanitic. Pressure on the mass elicited gurgling. A catheter when passed entered the urethra and then pointed directly downward along the anterior surface of the prolapse. Rectal examination showed that posteriorly the rectal pouch was likewise eventrated into the prolapse (Fig. 1).

Sedimentation time was thirteen minutes, hemoglobin 75 per cent, and the urine normal.

During the first night attempts at reposition made by the resident, after the patient had been placed in steep Trendelenburg posture and warm compresses applied, failed. The following morning I failed in all efforts which included pressure on the apex both before and after applying a rubber Esmarch bandage.

Signs of intestinal obstruction: enemas ineffectual, increasing abdominal pain, distention, nausea, no flatus passed, as well as increase of the edema and cyanosis locally and poorer general condition, forced me to perform an abdominal section twenty-four hours after admission, repeated attempts at reposition having failed. Because of the local infection and the presence of much intestine in the prolapse, the vaginal approach was rejected.

On opening the abdomen the great omentum was found adherent to the anterior abdominal wall over the pubis. Loops of small intestine were matted together by fibrin. On the right side of the abdomen the enormously distended and paper thin colon appeared to *descend* into the pelvis, blocking approach downward. Behind it were numerous loops of ileum which likewise entered into the pelvis. Some of these loops were readily drawn upward, several coming out of the extra-abdominal hernial pouch which formed part of the prolapse and extended more than halfway to the patient's knees.

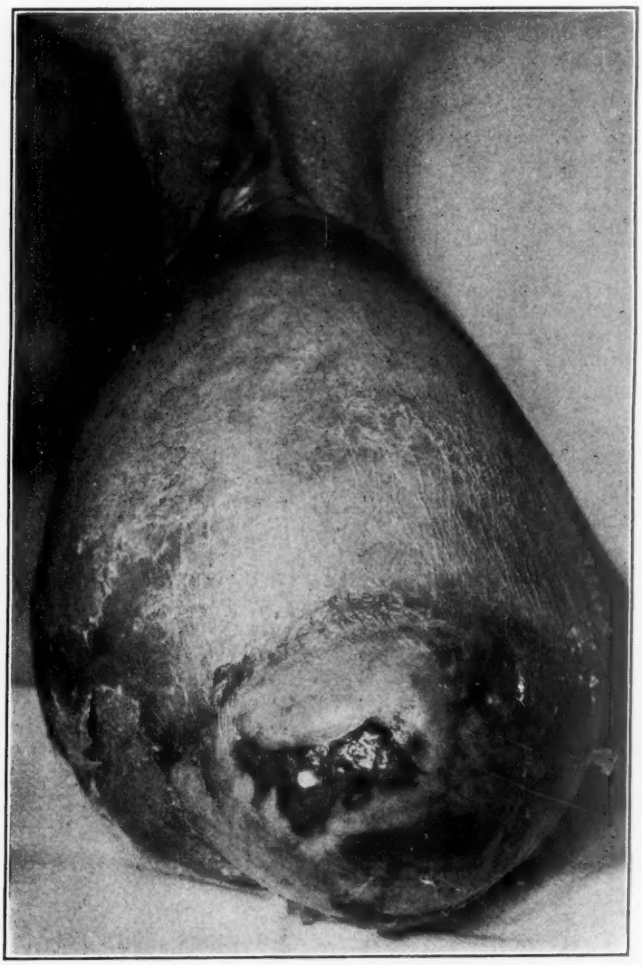

Fig. 1.—Prolapse with complete eversion of vagina.

In order to gain access to the pelvis and prolapse, after careful packing with moist compresses, a purse-string suture was placed on the distended bowel and through the center of this a large needle was inserted. Much gas was thus evacuated, and in the course of a few minutes the bowel collapsed. The needle was removed and the suture tied.

Now all accessible intestinal loops were freed and removed from the depths. The wall of one loop required repair. At the bottom of the sac which could only be reached by working the forearm downward, up to the elbow, an adherent transverse loop of collapsed ileum could be felt. Further exploration showed that the

peritoneum of the right side of the pelvis had slid or been pulled down, carrying the caput coli and appendix to the bottom of the prolapse. The uterus could not be felt.

Under visual control from within, two assistants made continuous, concerted pressure on the prolapse from the outside below, occasionally relieved by a third physician; after twenty minutes, the inversion suddenly occurred, the entire mass passing through the vulvar ring and rising into the abdomen. The mass was edematous and so large that it projected inches above the incision. The collapsed cecum, the appendix, and the adherent terminal loop of the ileum could be readily

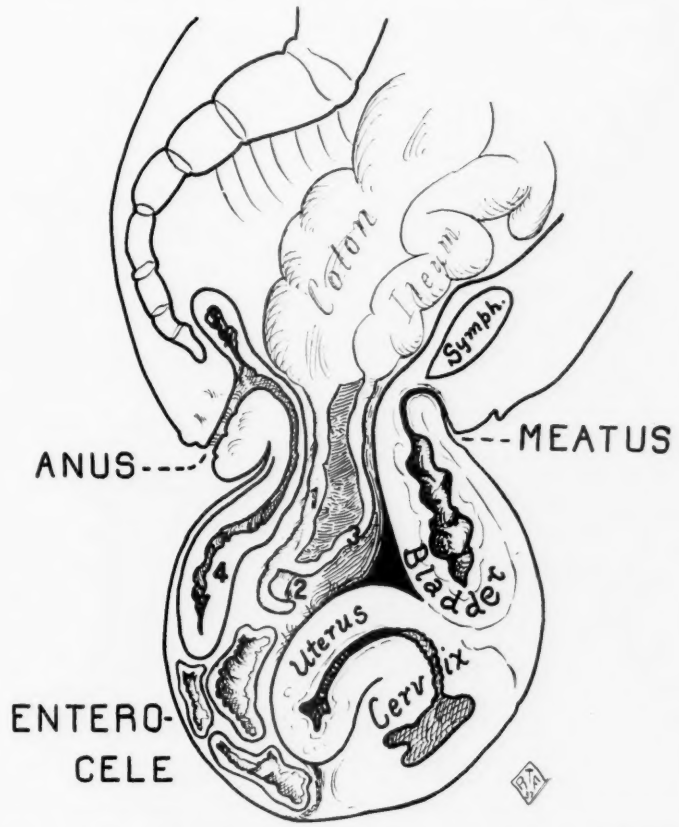

Fig. 2.—Schematic sagittal section through prolapse and pelvis. *1*, Collapsed cecum; *2*, appendix vermiformis; *3*, terminal ileum; *4*, lower rectum.

identified. The congested and thickened bladder likewise could be recognized but nothing of the uterus and adnexa could be seen because of adhesions. The abdominal wound was closed in layers with much difficulty, because of the excessive addition to the abdominal contents which overfilled the peritoneal cavity. Four laparotomy pads were packed into the vagina to prevent re-eventration of the prolapse.

The early postoperative course was stormy. Pneumonia and later a wound infection developed. After five days, however, the condition improved. The bowels moved spontaneously and the temperature fell. A tediously protracted, partly subfacial infection of the abdominal wound prolonged the convalescence. For eighteen days a pack was kept in the vagina to keep the cervix at a high level.

While the patient remained in bed, the cervix remained high, at least 2 inches above the ischial spines. The vagina was gaping, only a vestige of perineum. On the forty-first day, a week after the patient had been up daily, a second degree prolapse developed but was readily replaced.

Fifty-seven days after the laparotomy a typical parametrial fixation operation[2] was performed by me. The cervix at this time measured 3½ inches in diameter. The vaginal tissues and parametria were still edematous and boggy, the cervix of baconlike consistence. Convalescence was uneventful. Two and one-half months after this operation, conditions were found normal: cervix high, good perineum, and rather lax lateral walls. The patient is now fully cured for fourteen months.

The only case somewhat resembling the one I report, which I can find in the literature, and this patient did not survive, is one reported by Beyea[3] in 1898. He called it "A Case of Acute Septic Infection and Strangulation of a Completely Prolapsed Uterus; Vaginal Hysterectomy; Death." This was a 22-year-old Irish para iv who had had a prolapse for six years. For the four previous years she was unable to reduce it, and for six days there were chills and fever, the temperature rising to 103° F. At this time, for three days there were distention and vomiting. Catharsis proved ineffectual. On admission to the hospital, the temperature was 101° F. There was no distention. Vomiting was constant. The pulse was 120. Beyea found the prolapse the size of a child's head, of reddish blue color, with 2 ulcers, each the size of a dollar. Calomel was given and the bowels moved 6 times in twelve hours. The urine was clear. His attempts at reposition were unsuccessful. The temperature was now 100° F., the pulse 112 to 116, the patient was weaker, and the mass more cyanotic. No distention had developed.

Beyea performed a vaginal hysterectomy, encountering intestinal loops, congested and covered with lymph. His examination of the uterus showed small, multiple abscesses in the myometrium. The patient died five days after operation with all the symptoms of diffuse peritonitis.

In the literature Baldy's[4] case is frequently quoted in connection with Beyea's. Baldy's patient was seventy years old and found sudden enlargement of prolapse with pain and fever. The mass was twice as large as before. One-half of the mass showed ulceration and the entire prolapse was blackish in color. Baldy was able to reduce the prolapse completely after considerable difficulty. Seven days after the reduction he performed an abdominal operation (hysterectomy), there being fibroids present, fixation, and vaginal repair. This patient recovered.

Doubtless such cases as Slocum's[5] occasionally occur without being reported. This was a negress of 47 years who had suffered from long existing prolapse, which suddenly became irreducible and produced pain. The prolapse was 7 inches long and 19 inches in circumference. Slocum saw it shortly after the acute symptoms developed, and after the patient had been in the knee chest position for one and one-half hours, he succeeded in reducing the prolapse by manipulation. This patient was kept in bed three days.

One of the reasons that irreducibility of prolapse is rarely encountered is due to the fact that unless an extremely sluggish and unintelligent patient suffers from this trouble, the symptoms are so acute and violent that immediate help is sought. In the early stages before stasis and edema have occurred, reduction should always be possible.

The present case has been reported in such detail, because it appears to be the only patient who survived the severe abdominal operation necessary, and because the previous reports are incomplete. It is also hoped to draw attention to the fact that early reposition and retention of the prolapse is essential in order to avoid more serious consequences.

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1035 Park Avenue

ADENOMYOSIS IN A PRIMIPARA RESULTING IN SPONTANEOUS RUPTURE OF THE UTERUS AT THE ONSET OF LABOR*

MELVIN L. STONE, M.D., NEW YORK, N. Y.

(From the Obstetrical and Gynecological Service of the Third [New York University] Surgical Division, Bellevue Hospital and the Department of Obstetrics and Gynecology, New York University College of Medicine)

SPONTANEOUS rupture of the uterus in labor is a rare occurrence. Its incidence is variously estimated, but is probably in the proportion of about one case in 5,000 deliveries. DeLee[1] states that rupture is more often an accident among multiparas, and estimates that a ratio of 8:1 occurs in comparing multiparas with primiparas. A revised calculation of the frequency of spontaneous rupture of the uterus in primiparas appears to be about one case in 45,000 deliveries.

Most of the causes commonly assigned as responsible for spontaneous rupture of the uterus do not apply to the case here reported because they are based mainly on the theory that weakening of the uterine wall occurred as a result of frequent pregnancies or of previous operative procedures, such as myomectomy or curettage. Because it occurs so infrequently and because its pathogenesis is so interesting, the following case is recorded:

L. A., aged 25 years, colored, was admitted to the Bellevue Obstetrical Service at 8 A.M. Dec. 29, 1935, from another hospital. The patient had not attended a prenatal clinic. She stated that she was near term in her first pregnancy, the expected date being calculated as Jan. 6, 1936. She was awakened from sleep at 5 A.M. on the day of admission by pains recurring every five to ten minutes, lasting thirty seconds and not especially severe. For the past few weeks the patient said that she had to void urine about six times nightly, and on the morning of admission that she felt a continuous desire to empty the bladder.

Questioning failed to elicit any complaints other than the above. The patient denied any previous operation. The course of her pregnancy had been entirely uneventful.

Examination revealed a patient in good general condition. The pulse rate was 90 per minute, but the temperature was subnormal at 96.8° F. and later at 96.4° F. The blood pressure was 110/80. The heart and lungs were apparently normal. The abdominal examination revealed uterine and lower abdominal tenderness and some spasticity across the suprapubic region. The uterus was at the level of the umbilicus, a small firm projection being palpable at its upper pole. Fetal parts could not be outlined due to a fairly tense uterus, and several examiners were unable to hear the fetal heart. The patient insisted on lying on her side because it was painful to lie on her back. Rectal examination revealed a thick, closed cervix about 1 cm. in length. The presenting part was high and was believed to be a vertex.

Because of the urinary complaints and tenderness over the bladder region, the patient was immediately catheterized. The urine was cloudy, and contained innumerable polymorphonuclear leucocytes, and many small clumps of pus. The blood count revealed 23,800 W.B.C. with 86 per cent polymorphonuclear leucocytes and 2,710,000 R.B.C. with 60 per cent Hg. The blood was found to be Type 2.

A diagnosis was made of seven months' pregnancy with possible premature labor, and cystitis. The patient was given 2 gr. of sodium luminal to control pain. From this medication the patient became drowsy, slept at intervals, and did not complain greatly. The skin was cool and dry. The temperature 96.4° F.

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At 4 P.M. she complained of being cold and of difficulty in breathing. The respiratory rate was 22 per minute. She stated that she had no pain. The blood pressure was again taken and found to be 88/68. The patient vomited dark brownish material, which upon examination gave a three-plus benzidine reaction. Examination at this time showed that the patient was pale and the skin cold. The abdomen was markedly distended but soft, and tympany was present in the epigastrium and in the flanks. No fluid wave could be demonstrated and no Murphy sign was present. The uterus was apparently larger than in the morning, now reaching a point about two finger breadths above the umbilicus. It was exquisitely tender throughout and firm but not rigid. The small tumor mass noted on the fundus at a previous examination was still present. No fetal heart could be heard and the position of the fetus was believed to be R.O.A. Vaginal examination failed to reveal any bleeding; the cervix was effaced and one finger dilated. The fetal head could be felt high up and appeared to be small and soft.

The pulse rate was 120, and the temperature was 95.8° F. Because of the drop in temperature and in blood pressure, rise in pulse rate, pallor, moderate air hunger and anemia, as revealed by the red cell count, it was apparent that concealed bleeding was occurring. Although the uterus did not present the typical ligneous feeling, it was believed that the patient was suffering from premature separation of the placenta with uteroplacental apoplexy and concealed hemorrhage, and that intra-uterine death of the fetus had occurred. Because of the bloody vomitus it was also considered that the bleeding might arise from some extra-uterine source such as peptic ulcer, but this was not thought to be probable in view of the absence of fluid in the flanks, the small quantities vomited, the negative previous history, and the localized uterine tenderness together with evidence of fetal death. It was advised that laparotomy be performed immediately together with transfusion.

Accordingly, under gas-oxygen-ether anesthesia, the abdomen was opened and was found to contain about 1,000 c.c. of fluid blood and an approximately equal amount in the form of a stringy clot which filled the left gutter. The uterus was enlarged to the size of a seven and one-half to eight months' pregnancy and on casual inspection appeared to be normal. By palpation a soft mass about 6 by 6 cm. was felt on the posterior surface of the uterus and was believed to be the lowermost portion of the clot mentioned. The source of the bleeding was not at once apparent. The uterus was emptied through a midline incision in order to permit more thorough exploration. When this was accomplished and a small stillborn female child delivered, the uterus was brought through the wound. On its posterior surface there was a jagged perforation 5 cm. in diameter, extending through the entire thickness of the wall. Through this opening collapsed membranes protruded, and it was then realized that the mass palpated before delivery consisted of these structures. The blood clot previously mentioned was adherent around the edges of the perforation and near by the left tube and ovary were densely adherent, evidently the result of a preceding inflammatory process. The right tube and ovary were normal. The left tube and the uterus were removed, the pelvis peritonized, and the abdomen closed. The patient was given 700 c.c. of whole blood by the direct method, without reaction.

The patient's postoperative course showed a marked reaction. The temperature rose within the first twelve hours to 101.6° F. and by the third day was 104° F. It remained at this level for three or four days, falling to 103° F., where it persisted until the eleventh day postpartum. Transfusion of 500 c.c. of blood was given eighteen hours after operation and again on the fifth postoperative day; numerous gum-glucose infusions were utilized. The blood pressure, which was unobtainable immediately after operation and for three hours thereafter was 126/96 at the fourth hour, and subsequently was approximately normal. Tachycardia was present and persisted for the first three days, frequently being timed at 150 per minute, but on the fourth day it found a level commensurate with the temperature, and then slowly dropped. The cause of the postoperative reaction was believed to be the large quantity of intraperitoneal blood, since at no time was there any evidence of infection and the wound healed by primary union. A blood culture taken on the fifth postoperative day was reported as containing a few colonies of *Staphylococcus aureus* (probably contaminant). Vaginal culture revealed gram-positive bacilli and cocci

and gram-negative bacilli. No hemolytic microorganisms were present. The patient was discharged in good condition on the twenty-first postoperative day.

Pathologic Report.—(No. 4571/35.) The organs removed were examined macroscopically and histologically and the following report was given (Drs. W. E. Studdiford and H. Salter):

Macroscopic Examination: "Specimen consists of a uterus measuring 22 by 18 by 6 cm. The external surface is covered with a smooth pinkish-yellow serosa. Anteriorly there is a 6 inch surgical incision extending from the cervical to the fundal portion in the midline, the edges of which are approximated by catgut sutures. Posteriorly in the central fundal portion is a ragged, hemorrhagic perforation, which extends from serosa to endometrial surface. This opening is about 3 cm. in diameter. The tissue surrounding the opening appears similar to that of the rest of the uterus. On the left lateral aspect of the opening is the attachment of the round ligament to which is attached the folds of the broad ligament. The right round ligament is not present.

"On removal of the surgical sutures, the uterine walls are seen to measure 4 cm. anteriorly; posteriorly in the region of the above described defect, the musculature

Fig. 1.

measures 1.5 cm. in thickness and becomes thinned and more hemorrhagic toward the edges of the opening. The uterine cavity is lined by ragged, shaggy, pinkish-yellow tissue, stripping easily, which appears to be decidua. The interior of the uterine cavity near the perforation is striking in that there is a deep crevice in the tissue which measures 3-4 cm. in length and several mm. in depth, becoming deeper and broader as it approaches the inferior aspect of the opening with which it is continuous. There are several smaller crevices situated radially about the defect.

"On the anterior serosal aspect is a 2 cm. pedunculated tumor resembling a fibromyoma, the pedicle of which is 1 cm. in length."

Microscopic Examination: "Sections of the uterus show areas of smooth muscle cells formed into bundles and running at various angles. The muscle bundles, as well as the individual cells, are separated from each other by clear spaces appearing to contain fluid. The cytoplasm of the muscle cells is pale and shows many vacuoles. There appears to be a hyperplasia of the smooth muscle cells. The endometrial surface of the musculature is covered by decidual tissue consisting mostly of the glandular layer with no chorionic villi seen. There are also several large areas of old red blood cells in the tissue and areas of fibrin. A good many infiltrating polymorphonuclear leucocytes are seen in this latter tissue."

"In all sections throughout the musculature are seen clear areas lined by a thick layer of decidual tissue consisting of both compact and glandular layers of cells. (See Fig. 1.) This tissue is seen both close to the rupture and at a distance from it."

Diagnosis: Hyperplasia and edema of uterine musculature, rupture of the uterus, pedunculated subserous fibromyoma uteri, and adenomyosis uteri.

DISCUSSION

In the literature are reports of many ruptured uteri from a variety of causes. There are in addition many reports of adenomyosis. It seems strange that so few cases of rupture caused by adenomyosis should have been recorded. Marinacci[2] reports a case of rupture of the uterus following invasion of a cesarean scar by chorionic villi, that is similar to our case, but the cause of which is not so clear since two factors play a part. Aschheim[3] mentions adenomyosis in a pregnant uterus with fibromyoma, as indeed do many others, but in Aschheim's case the pregnancy was not far advanced (about four months) and rupture did not occur. After a search of the literature only one case was found similar to the one here reported. The case in question was published by Richardson.[4] Unfortunately no clinical history is given, the entire report being concerned with the pathologic findings in a case of spontaneous rupture of the uterus. The similarity of the two cases can best be appreciated by reference to the pathologic report, which is reproduced verbatim:

"Specimen is a uterus which had ruptured longitudinally on the anterior superior surface. The edges of the rupture are covered with a rough, dark red, friable material, apparently organizing blood clot, and section of the adjacent uterine wall shows an irregularly mottled red and white surface. No evidence of the scar of a former cesarean section is found. Microscopic sections taken at the edge of the rupture show uterine tissue with the characteristics of pregnancy. There is, in addition, a very considerable infiltration of the wall with decidual cells, extending deep into the muscle tissue. Some increase in connective tissue is also found. While it cannot be said that the infiltration was the cause of the rupture, the coincidence forces one to the belief that it was at least possible."

It is probable that the interpretation of Richardson's[4] case in the light of the scanty knowledge of adenomyosis at the time of its publication, was somewhat different from the interpretation now generally accepted. Its title, "Ruptured Uterus With Decidual Cell Infiltration of Uterine Wall," seems to indicate that it was supposed that the invasion of the uterine wall took place after nidation owing to some abnormal stimulus to the cells themselves by pregnancy. With the current theories as to the pathogenesis of adenomyosis it becomes clear that the so-called invasion of the uterine wall is in reality the development of the changes of pregnancy in aberrant endometrium. This is supported by the findings, in our case, of numerous foci of decidual cells at a great distance from the endometrium and apparently having no direct connection with it, which connection, it must be supposed, would exist were direct invasion the pathogenetic factor. Further, the findings in cases of adenomyosis which are not complicated by pregnancy, seem to bear out this theory.

SUMMARY

An interesting and rare case of spontaneous rupture of a full-term primigravid uterus at the onset of labor is reported. The patient had had no previous operative manipulations of the uterus and by subsequent microscopic examination, and at operation it was demonstrated that adenomyosis was responsible for the rupture.

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239 Central Park, West

PYELITIS OF PREGNANCY DUE TO THE BACILLUS DYSENTERY FLEXNER

H. L. Stewart, M.D., Detroit, Mich.

(From the Department of Gynecology and Obstetrics, Henry Ford Hospital)

REPORTS of only two cases of pyelitis due to the Flexner type of dysentery bacillus complicating pregnancy have been published. The treatment was different in each case. In the case herewith presented mandelic acid was used. The ketogenic diet is also considered.

M. D., a white female, aged 20, was admitted to the Henry Ford Hospital Dec. 12, 1936. Chief complaints on admission were: pain in both kidney regions, generalized abdominal pain, persistent nausea and vomiting, frequency of urination, dysuria, loss of weight and strength. All symptoms were present three and one-half weeks. The last menstrual epriod was July 15, 1936. The estimated duration of pregnancy was five months. Occasional backache, frequency of urination, and dysuria were first noted at the end of the second month of pregnancy. Independent of treatment, a slight temporary improvement of symptoms was present until the beginning of the fourth month when pain and dysuria returned with greater severity. This was soon followed by chills, fever, generalized abdominal distress, nausea and vomiting. Within the next week, she was confined to bed with persistent vomiting, loss of weight, abdominal pain, chills, fever, and extreme weakness which continued until admission to the hospital.

The family history is irrelevant. The past history is not significant. Appendectomy was performed at the age of thirteen with an uneventful recovery, otherwise, she never had symptoms referable to the gastrointestinal tract and claimed good general health.

Positive findings on physical examination were: temperature 104.4° F., pulse 156, respirations 24, blood pressure 96/50. The patient appeared very toxic and the dry skin presented evidence of dehydration. She was 20 pounds underweight. The face was thin and drawn. Mucous membranes were pale. Dental caries was present. Tongue was coated and dry. Lungs were clear. Heart was normal. Fundus of uterus extended 15 cm. above the symphysis pubis. Fetal movements were seen and felt. No other organs or masses were palpable. There was generalized abdominal tenderness as well as extreme tenderness in both costovertebral angles. She was critically ill.

Laboratory findings were: Hemoglobin, 60 per cent; R.B.C., 3,050,000; W.B.C., 22,000 with 87 per cent polymorphonuclears and 13 per cent lymphocytes. Catheterized urine showed specific gravity 1.020, acid reaction, trace of albumin, many pus cells, occasional red blood cell, no casts and tests for sugar, acetone and diacetic acid were negative. Centrifuged specimen: stained sediment showed many pus cells and many Gram-negative bacilli, identified as the Flexner bacillus of dysentery. Patient's serum agglutinated the Flexner bacillus in a dilution of 1:640 but was negative for the typhoid-paratyphoid groups. Stool cultures were negative for dysentery organisms. Blood chemistry showed: CO_2, 44.7 vols. per cent; non-protein nitrogen, 22.0; chlorides, 450. Blood serology negative.

Because she was unable to retain fluids by mouth, parenteral fluids were forced for the first thirty-six hours of hospitalization. Two days after admission, she tolerated a liquid diet. Mandelic acid therapy was instituted by giving 12 gm.

daily supplemented by 30 gr. of ammonium chloride in enteric coated tablets. Initial urinary pH was 5.9. By December 17, the temperature was normal, but clinically the patient showed only slight improvement. On December 19, chills, fever, nausea, and vomiting returned. Daily temperature ranged between 100 and 104° F. Although a urinary pH of 5.0 had been maintained since the beginning of treatment, the urine contained many pus cells and the Flexner organism was again isolated. Additional laboratory studies showed: blood chemistry within normal limits. Phenolsulphonphthalein test showed 45 per cent excretion in one hour. Roentgenogram of abdomen revealed nothing abnormal. Retrograde urograms demonstrated bilateral dilatation of ureters and kidney pelves. Bromsulphalein liver function test showed 5 per cent retention in thirty minutes.

The management of this case was again carefully considered. The ketogenic diet was not applicable for a high carbohydrate, high caloric diet seemed indicated on account of high fever, loss of weight and strength, and evidence of beginning liver damage. In addition, there was anorexia, nausea, and vomiting. A ketogenic diet was, therefore, not practical. Therapeutic termination of pregnancy was considered. It was decided, however, to continue the mandelic acid therapy which was supplemented by ureteral catheterization and drainage of both kidney pelves, the latter being performed twice weekly. In addition, the patient received four blood transfusions of 350 c.c. of citrated blood.

On January 11, the patient developed an acute tracheobronchitis. Chest x-rays were negative for evidence of consolidation. Consultation with the General Medical Staff regarding the physical condition and with the Urologic Staff regarding the renal status, brought the recommendation of therapeutic termination of pregnancy as the final step to save the life of the patient.

The following day the membranes were ruptured. Labor followed eighteen hours later. Spontaneous delivery of a living, female child terminated an eight-hour labor. The child had not reached the age of viability and, consequently, lived but a few minutes. The placenta readily separated by the Schultz mechanism five minutes later. Estimated blood loss was 50 c.c.

Following delivery the temperature ranged between 100 to 102° F. for thirty hours but thereafter dropped quickly to normal limits where it remained during the subsequent nine days of hospitalization. The recovery was astounding. She immediately tolerated a full diet with a rapid gain of appetite, strength, weight, and showed general clinical improvement. Renal tenderness quickly diminished to slight residual soreness although the urine contained the Flexner organism and a moderate number of pus cells. Rapid improvement continued. When last seen in April, 1937, her general physical condition was excellent. She no longer presented symptoms referable to the urinary tract.

In a review of the literature, Calalb and Jonesco, in 1915, reported the first case of pyelitis due to the bacillus dysentery Flexner complicating pregnancy. They reported satisfactory results by treatment with autogenous vaccine.

Cheatham, in his case report with a review of the literature to 1934, cites only the case of Calalb and Jonesco. Cheatham's case was a multiparous woman in the seventh month of pregnancy complicated by pyelonephritis due to the Flexner organism. The patient spontaneously delivered a living female child of eight months. Profuse postpartum hemorrhage following the third stage of labor, indicated transfusion. With a very satisfactory convalescence, the temperature returned to normal by the seventh postpartum day. They were especially interested in the use of bacteriophage therapy which proved of little value. Vaccines were avoided because of the negative phase. Urinary antiseptics could not be used due to the unusual vomiting. The clinical value of mandelic acid therapy had not been recognized. They attribute the rapid improvement of their case to the use of postpartum blood transfusions.

In our case, vaccines and bacteriophage were not given a trial for we relied upon the use of mandelic acid combined with adequate renal drainage. Mandelic acid treatment of pyelitis of pregnancy due to the colon bacillus has been very satisfactory, but in this case it did not affect the Flexner organism. Several blood transfusions were given prior to therapeutic induction of labor without appreciable results, which is not in accord with the experience of Cheatham. Furthermore, the postpartum course of our patient showed a rapid cessation of all symptoms independent of blood transfusions and specific medication to the urinary tract. A further contrast to Cheatham's case was the absence of postpartum hemorrhage.

SUMMARY AND CONCLUSIONS

A rare case of pyelitis of pregnancy due to the bacillus dysentery Flexner is reported. The organism was isolated from the urine on several occasions and identified by the usual cultural characteristics. The organism was agglutinated by known antiserum. The patient's serum agglutinated the Flexner bacillus in dilutions 1:640 but was negative for typhoid-paratyphoid and other dysentery organisms. Stool cultures were negative for Flexner bacillus.

Mandelic acid therapy alone and later supplemented by adequate drainage of kidney pelves proved unsatisfactory in this case in contrast to experience with pyelitis of pregnancy due to the *Escherichia coli.*

In view of the severity of the infection and the clinical course prior to therapeutic induction of labor, the ketogenic diet was contraindicated for the patient.

On the recommendation of two consultants, pregnancy was terminated, which proved to be a lifesaving procedure for the mother. Postpartum convalescence was rapid and independent of treatment; therefore, any form of therapy during this time must not be regarded as specific.

BILATERAL OVARIAN DERMOID CYSTS

With One Dermoid Containing an Appendix and a Portion of Ileum

Lewis E. Schottenfeld, M.D., C.M., and Emanuel V. Littauer, M.D.,
Brooklyn, N. Y.

(From the Departments of Gynecology and Surgical Pathology, Jewish Hospital.)

THE following case is unique as a pathologic rarity and worthy of record.

K. S., a housewife, aged 39, was admitted on Feb. 1, 1935 to the Gynecological Service of Dr. Leo S. Schwartz at the Jewish Hospital of Brooklyn with the following history:

She complained of severe pain in the right lower part of the back and intermittent vaginal bleeding of two months' duration. Family history was irrelevant. Past history: married fifteen years, gravida iii, para ii, and one miscarriage at four months. She had frequent attacks of dyspnea on exertion with mild cyanosis and ankle edema. The history of her weight development coincident with her menstrual history revealed a definite endocrine influence. During the stage of puberty she was a puny girl. At 25 years she weighed 145 pounds; five years later her weight increased to 200 pounds. At the time of her admission to the hospital she weighed 225 pounds. Her maximum weight was 243 pounds. Her menses had always been irregular and were accompanied by premenstrual pains. At 26 years she had a period of amenorrhea during which her weight reached 222 pounds. With a proper diet her weight decreased to 160 pounds, after which her menstrual periods again recurred at intervals of two and three months. At 37 years she had another period

of amenorrhea which lasted six months and again her weight increased. During this time she suffered severe headaches and developed a hypertensive state. Following thyroid medication for her obesity, her headaches became less severe and her menses reappeared but in irregular fashion.

Present Illness.—For two years prior to her admission to the hospital her menses were infrequent and scanty. She was free from symptoms until two months before her admission when her menses recurred. The flow at this time lasted seven days and was accompanied by intense stabbing pains in the lower part of the back, the right lower quadrant, the thighs and calves of the legs. After an interval of two days she again began to bleed. This bleeding lasted another seven days and was accompanied by similar pains. From then and continuing to the time of admission, she bled every other week. This was accompanied by severe abdominal pains, headaches, dizziness, nausea, blurring of vision, and chills. There was no change in the urinary or bowel habitus.

Physical Examination.—Revealed a very obese, plethoric woman, who seemed at ease and not acutely ill. The heart was enlarged to the left and right, and a soft blowing systolic murmur, which was not transmitted, was heard at the apex. The blood pressure was 180 systolic and 100 diastolic. The abdomen disclosed a thick panniculus arranged in large folds which hung down to the knees. On deep palpation, indefinable masses were felt in both lower quadrants of the abdomen. Both ankles were markedly swollen and there were numerous varicose veins on both legs. Pelvic examination: revealed a lacerated pelvic floor and cervix; a movable, very tender and semicystic mass was palpated in the cul-de-sac which, by bimanual examination, extended to four fingerbreadths below the umbilicus; another large mass was palpated more anteriorly on the right. A diagnosis of bilateral ovarian cysts was made. The laboratory data were as follows: the blood sugar content was 192 mg. per 100 c.c. of blood; the Wassermann and Kahn tests were negative; urinalysis was repeatedly negative. The blood count showed over 5 million red blood cells, hemoglobin 74 per cent (Dare), white blood cells 12,800, with 74 per cent polymorphonuclear neutrophilic leucocytes, 21 per cent lymphocytes, 4 per cent monocytes, and 1 per cent eosinophiles.

Operation.—On Feb. 5, 1935, under spinal anesthesia, the abdomen was opened through a lower paramedian incision. Bilateral ovarian cysts were exposed. The right was nodular and appeared dermoid in character. It was as large as a good sized grapefruit, with half a twist of the pedicle, but freely movable in the pelvis. The round ligament was adherent to it. The cyst on the left was about half the size of the one on the right and situated behind the uterus in the cul-de-sac. It likewise appeared to be a dermoid. The uterus, lying between both cysts, was small. A supracervical hysterectomy and bilateral salpingo-oophorectomy was performed and the cervical stump peritonized. An appendectomy was also performed. During convalescence, the temperature remained normal with a rise to 101.6° F. on one occasion. The blood pressure gradually declined to 130 systolic and 80 diastolic. She recovered uneventfully and was discharged on Feb. 26, 1935, three weeks postoperative.

Pathologic Report.—The specimens consisted of the appendix, the uterus, tubes, and bilateral ovarian tumors. The uterus and tubes appeared normal. The surface of the appendix appeared smooth and gray, and the mucosa and muscular wall were normal. The smaller of the two ovarian tumors was spherical and measured 8 cm. in diameter. The surface was smooth and gray pink. The contents consisted of thick, yellow, butterlike material intermixed with hair. A small mass present in one portion of the cyst was incorporated in the wall and when sectioned consisted of osseous and adipose tissue. The larger tumor (Fig. 1) measured 16 cm. in diameter. The contents resembled that of the smaller tumor, with a large amount of thick, yellow, opaque, mucinous material. A pedunculated bean-shaped mass attached by one pole to the inner surface of the cyst, consisted of a central mass of red tissue surrounded by yellow fatty tissue. In another part of the wall was an irregular swelling which projected in the form of several nodules which were hard, yellow and pink, and appeared to be bone.

On further dissection of the large dermoid, another compartment was disclosed, and the wall which separated this from the main cyst cavity was markedly thickened. In the smaller loculus was a segment of intestine 14 cm. long and 3 cm. in

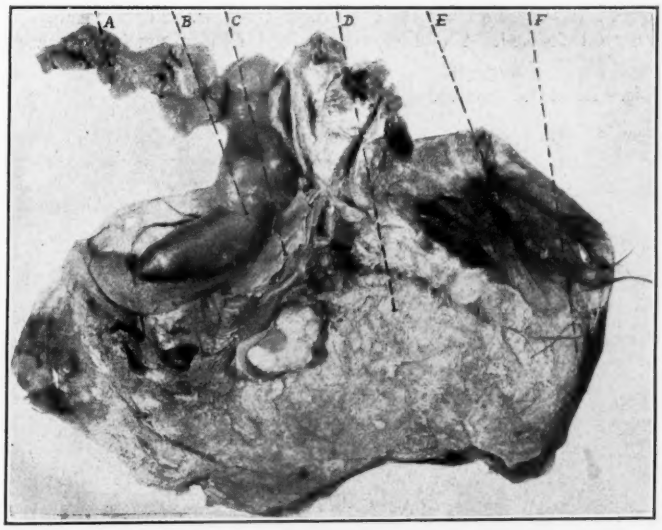

Fig. 1.—Gross specimen. *A*, Appendix in cyst; *B*, small intestine in cyst; *C*, cut edge of smaller cyst compartment; *D*, grumous material; *E*, hair; *F*, cut edge of large cyst proper.

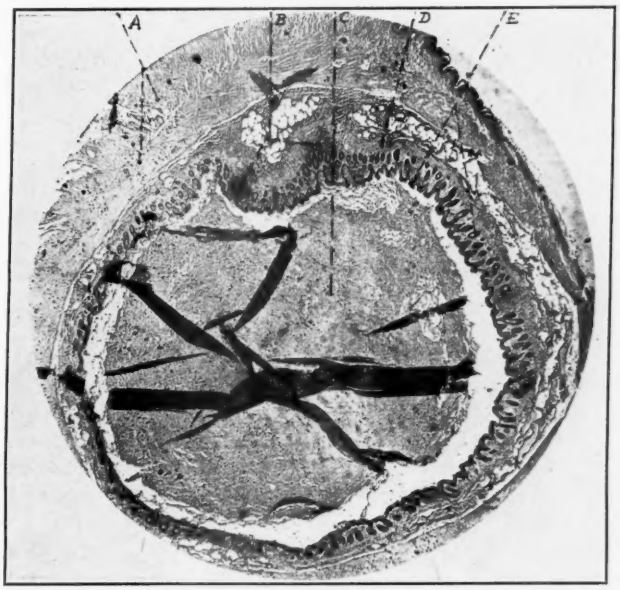

Fig. 2.—Gross specimen of appendix within cyst. *A*, Muscular layer; *B*, lymph follicles; *C*, cellular and amorphous debris in lumen of appendix; *D*, submucosa; *E*, mucosa with mucosal glands and tubules.

diameter. One-half the length of this intestine had the appearance of ileum, and the other half, the caliber of which was much narrower, closely resembled a vermiform appendix with a rudimentary mesentery attached.

Microscopic.—The uterus, tubes, and appendix showed no pathologic changes. A variety of tissues was recognized in both tumors: viz. bone, muscle, and fat. A section of the appendiceal structure, lying within the cyst (Fig. 2), revealed the various layers of the appendix. The mucosa was intact, and the submucosa contained several immature and one mature lymph follicles. The muscular coat and the serosa were well formed. The lumen contained débris, mucinous material, and a few cells.

Diagnosis.—Bilateral dermoid cysts of the ovaries.

PLACENTA ACCRETA

CLARENCE B. SACHER, M.D., DALLAS, TEXAS

MRS. L. P., a white American multipara, aged 31 years, was admitted on my services at Dallas Methodist Hospital, Sept. 2, 1936. Her first pregnancy was normal in all respects; she delivered an 8-pound girl on Sept. 12, 1933. On the present occasion she started labor at 5 A.M. and entered the hospital at 6 A.M. She was in first stage of labor, having pains every five minutes, duration one minute, and a cervix effacing with 2 cm. dilatation. At 9 A.M. pains were every two minutes and lasting one minute. At 10:30 A.M. the cervix was completely dilated. One hour later midforceps were applied, and a normal live 9 pound girl baby was delivered. Thirty minutes later the placenta had not delivered, and Credé's method was unsuccessful. A short mediolateral episiotomy was repaired. Because the placenta would not be expelled under normal methods, it was decided to keep the patient on the delivery table, taking all precautions against infection. The cord with forceps clamped on one end was wrapped in a sterile towel and laid on the abdomen. 1,000 c.c. of 5 per cent glucose was given intravenously, also ¼ gr. of morphine. Later examination revealed that the uterus remained stationary in the abdomen, and the placenta could be palpated in the fundus. There was no flow, no rise of the globular fundus uteri, and no descent of the cord. The patient was in good condition. A diagnosis of placenta accreta was made without an intrauterine examination. The patient was prepared for operation while donors for a blood transfusion were obtained. She had been asleep since 9 A.M. under nembutal. At operation a supravaginal hysterectomy and appendectomy were performed. Immediately after the operation the patient was given 470 c.c. of whole blood by the direct method. The patient was in good condition when removed to her room. The temperature went up to 100° F. for two days, after which it was normal. The next day after operation, the patient said she felt fine and believed she could get up. She made an uneventful recovery and was discharged from the hospital on the eighth postoperative day.

The patient was given her final examination January, 1937, some four months after the delivery. She stated at that time that she had had no aches or pains, or any nervous symptoms. Examination revealed a healed perineum and normal pelvic organs. She was discharged as well.

On opening the uterus after operation the placenta was normal to look at except that there was no separation from its attachment in the fundus of the uterus between both cornu. No line of cleavage for separation could be made manually. The pathologic report made by Dr. J. L. Goforth is as follows:

Gross Examination.—The supracervical portion of the uterus was symmetrically enlarged and measured approximately 14 by 12 by 12 cm. A few scattered fibrous adhesions were present about the posterior portion. On being opened the myometrium showed much hypertrophy. The endometrial cavity contained a term-

sized placenta which measured 14 by 14 by 13 cm. This organ was so tightly adherent to the uterine wall that it could not be pulled away. The fetal surface, cord, and fetal membranes grossly were not remarkable. On section through the placenta an unusually firm union between placenta and uterine wall appeared to exist. On gross study it could not be determined with certainty whether the decidua basalis was present or not. The placental tissue itself showed no degenerative changes grossly. Throughout the body of the organ localized hemorrhagic areas 1 to 2 cm. in diameter were demonstrable. The myometrium from the gross point of view could not be said to be invaded by placental tissue.

Microscopic Examination.—Sections through different portions of the placenta, the sections being taken so as to show both placenta and myometrial tissue, showed that the chorionic villi were normally firm. The muscle fibers of the myometrium

Fig. 1.—Section of tissue showing the absence of decidua basalis and invasion of the myometrium by chorionic villi.

were tremendously hypertrophied. There was practically no decidua basalis tissue between the placenta and myometrium. Here and there a small irregular patch of decidual cells was noted but a decidual layer could not be made out. The myometrium was moderately well invaded by chorionic villi. From the microscopic point of view this invasion was sufficiently well established to account for the adherence of the placenta to the uterine wall in terms of nonseparation. The sections revealed no evidence of malignancy and the invasion described did not extend very deeply into the myometrium. Here and there the myometrium itself seemed to peninsulate into the placental tissue. The union between the placenta and myometrium was usually firm at these sites.

Pathologic Diagnosis.—Postpartum uterus with adherent placenta (placenta accreta).

819 Medical Arts Building

CEREBRAL COMPLICATIONS FOLLOWING NITROUS OXIDE ANESTHESIA

HARWIN BROWN, M.D., GLENN COLLINS, M.D., AND
FRED K. VAUGHAN, M.D., OKLAHOMA CITY, OKLA.

(From the Departments of Obstetrics and Anesthesia, State University Hospital)

DURING the past few years several articles in the literature have presented cases showing evidence of nervous tissue damage following nitrous oxide anesthesia. Most authors have believed the injury due to anoxemia; a few have suggested that idiosyncrasy may play a part. We feel unentitled to a definite belief in the two or more sides of this controversy. The articles by Courville[1] and by Löwenberg and others[2] with the bibliographies of each are references aplenty for those interested. Our own case follows fairly well those already published.

An 18-year-old para 0, gravida iii was admitted to the hospital in labor at 8:45 P.M. on Jan. 15, 1937. Her prenatal record showed a normal pregnancy. On admission blood pressure was 120/80, presentation was cephalic, and station was -1.

At 11 P.M. 1/6 gr. of morphine and 1/150 gr. of scopolamine were given. At 1:30 A.M. she was taken to the birth-room apparently well sedated. N_2O and O_2 anesthesia was begun by the interne on anesthesia service at 1:40 A.M. Her pulse was 124, respiration 20. Induction required 92 per cent N_2O and 8 per cent O_2, was rather slow. During the following eight minutes N_2O concentration varied between 92 per cent and 80 per cent. At 1:48, following episiotomy, a normal, slightly narcotized infant was delivered by means of low forceps. The patient was awakened, talked freely, named her baby, and appeared normal in every way.

Ergotrate gr. 1/320 was given intravenously, the placenta delivered at 1:58 A.M.; anesthesia again was induced with about 92 per cent N_2O, and continued with about a 9:1 gas-oxygen ratio. During the ensuing minutes respiration became slow, shallow, and labored on two occasions, each time responding quickly to an increase in O_2. At 2:20 A.M., about twenty-two minutes after the second induction, respiration became labored, irregular, did not respond to 100 per cent O_2, and finally ceased altogether. The patient became markedly cyanotic, the pupils dilating widely, the eyeballs fixing in the central position. On administration of 100 per cent O_2 under pressure the patient's color returned, but respiration was gasping, irregular, and very slow. The pupils were contracted. The tongue at no time seemed to obstruct the pharynx, but an air-way was inserted and tolerated. Metrazol, an analgesic, 1 c.c. was given intramuscularly at 2:26 A.M. and repeated intravenously at 2:39 without immediate benefit to respiration. A small amount of vaginal bleeding was noted and 1 c.c. of pituitrin was given intramuscularly. At 3:15 the pulse was 150, the blood pressure 180/80, respiration 15, and the rectal temperature 100°. Oxygen 100 per cent was discontinued, but of necessity resumed immediately, small amounts of CO_2 being added. Eyeball movements were active; the lid reflex returned. The patient seemed conscious, but did not respond to her surroundings nor to ordinary stimuli. By 3:28 A.M. respiration, though still irregular, seemed of better quality, rate 28. At 3:40, 1 c.c. of metrazol was given intravenously; ten minutes later respiration was regular and deeper. Blood pressure was 130/90. At 3:55 it was found that O_2-CO_2 were no longer necessary. At 3:30 reflexes had been found to be very sluggish, but at 4:00 A.M. the patient began to show a spasm of the upper extremities similar to carpopedal spasm. All reflexes became active. Seizures developed and were repeated every five to ten minutes, characterized by movement of the head from side

to side, flexion of both arms with carpal spasm, marked spasticity of both lower extremities with bilateral Babinski phenomenon, and a wide frightened expression in the eyes. There were some clonic movements of the upper extremities. Mild opisthotonus was present at intervals. The patient was returned to bed at 5:30 A.M. where she soon became so wild and noisy that sedation was necessary. At 11 A.M., Jan. 16, 1937, the temperature was 102°, pulse 140, and respirations 22 to 44.

Neurologic and neurosurgical consultation gave an impression of "diffuse cortical and basal ganglion cell injury." The patient's neurologic condition changed but little until death on Feb. 5, 1937. Temperature at death was 106.8° F. per rectum.

Treatment had included morphine, 10 per cent and 20 per cent intravenous glucose, parathyroid hormone and calcium levulinate intravenously, resulting in transient improvements. Oropharyngeal O_2 was used for a few days when pneumonia threatened on Jan. 26. Feeding by stomach tube was necessary throughout most of the illness. Incontinence was the rule. Autopsy was not permitted. Urinalysis, blood counts, blood chemistry, and spinal puncture were all essentially negative through the postpartum course.

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RUPTURED EXTRAUTERINE PREGNANCY COMPLICATING UNUSUALLY LARGE MULTIPLE FIBROIDS OF UTERUS

A. J. GORDON, M.D., F.A.C.S., NEWARK, N. J.

RUPTURED extrauterine pregnancy is occasionally seen associated with small fibroids, usually solitary, of the uterus, but a case seen in conjunction with large multiple fibromas is worthy of reporting.

M. R., negress, aged 32 years, no children, with a history of one pregnancy years ago terminating in a three months' spontaneous abortion, was admitted to the gynecologic service of Dr. Wm. Gauch at the Newark City Hospital, with pain in the lower abdomen and an amenorrhea of two months' duration as her chief complaint. The patient was first seen in consultation with the Medical Service of the hospital, to which service the patient was originally admitted for a supposed respiratory disorder; the diagnosis of an acute surgical abdomen was made, and laparotomy was decided upon.

Physical Examination.—Well-developed negress, apparently in acute pain, centered in lower portion of abdomen; temperature 100, pulse 90, respiration 22; blood pressure, 132/80; W.B.C., 9,850, polymorphonuclears, 86 per cent; R.B.C., 3,800,000; Hg, 55 per cent; urinalysis essentially negative.

Head and chest showed no pathology.

Abdomen: Tenderness and some rigidity over entire lower abdomen; large multiple fibroids felt, one extending to three fingerbreadths above the umbilicus on the right, and on the left large nodules extending to the umbilicus and completely filling the pelvis.

Vaginal Examination.—Perineum not relaxed, cervix soft, numerous large fibroids completely filling the pelvis and extending upward above the umbilicus, no tenderness in the fornices.

Rectal Examination.—Confirmed vaginal examination.

Operation.—Lower median incision into the peritoneal cavity revealed some free blood. In the entire lower abdomen and extending above the umbilicus were numerous large fibroids as large as full-term fetal heads. The left tube was compressed between a large fibroid and lateral wall of the pelvis. Upon freeing the tube there was a rent in its outer third, between the isthmial and ampullar portion from which protruded a fetus and placenta. The left tube was removed, leaving the left ovary.

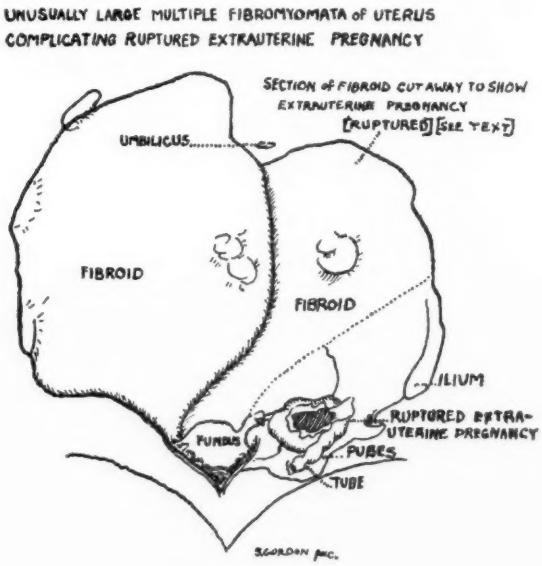

Fig. 1.

Nothing else was done. The abdomen was closed without drainage, and the patient made an uneventful recovery, and will return at a future date for a hysterectomy.

Comment.—The compression of the left tube between one of the fibroids and the lateral wall of the pelvis accounted for the small amount of free blood in the peritoneal cavity and, consequently, the patient's not showing marked signs of internal hemorrhage.

351 Roseville Avenue

Hudson, Alfred E. A.: A New Technic for the Examination of Trichomonas Vaginalis, Malayan M. J. **12**: 73, 1937.

A simple method of demonstrating the *Trichomonas vaginalis* consists in obtaining a drop of vaginal secretion by means of a pipette or medicine dropper and placing it on a warm slide, on which is a drop of warm saline solution. The protozoan parasites, if present, will be recognized by their rapid, jerky motions, swimming to and fro. Dark-field examination is not necessary.

Various morphologic types have been described by Goddall: pineapple, windmill, angler, spin-wheel and the seal. Mixed types are not usually found in the same case.

F. L. Adair and S. A. Pearl.

SPONTANEOUS FRACTURE OF THE FEMUR IN THE NEONATAL PERIOD

EDWARD L. CORNELL, M.D., F.A.C.S., CHICAGO, ILL.

SPONTANEOUS fractures which occur in the neonatal period are sufficiently rare to warrant reporting a case. A young woman, 28 years of age, reported in her third month of pregnancy. At that time nothing abnormal was noted. Her family history was non-essential, as were her previous illnesses. The Wassermann and Kahn tests were negative, and the blood count was within the normal. She reported

Fig. 1.

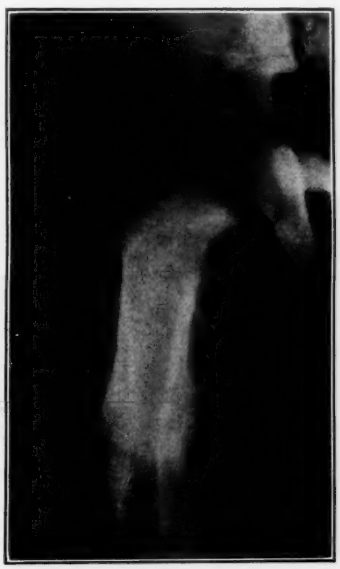

Fig. 2.

Fig. 1.—Fracture of the femur as seen by x-ray, June 29, 1936.
Fig. 2.—Fracture of the femur as seen by x-ray, Sept. 10, 1936.

to the office regularly at the usual prenatal intervals. There was no finding of significance, except that she had gained more weight than the average patient. The highest blood pressure reading during pregnancy was 120/70; the urinalysis was normal.

She entered labor spontaneously one day after the menstrual due date. After twenty-one hours in the first stage of labor, she delivered spontaneously, having a forty-five-minute second stage of labor. The baby, a female, was perfectly normal, weighing 3170 gm. The baby nursed and was given supplementary feedings. The patient was to be discharged on the twelfth day.

On the evening of the eleventh day, the baby was taken to the mother for its 10 o'clock feeding and was in excellent condition. It was placed in the crib, and nothing wrong was noticed by the night nurse until about 5:00 A.M., when she heard the baby cry loudly. She picked the baby up at that time to prepare it for the

6:00 A.M. feeding and noticed that it could not move its right leg. She took it in to the mother for nursing, and at 7:00 A.M. she called the interne. He found the right leg to be fractured in the middle third of the femur. Upon my arrival in the hospital at 9:00 A.M. I found the leg was broken. An x-ray was ordered and Fig. 1 shows the right femur fractured at the middle one-third, the proximal fragment overriding anteriorly. The condition of the other bones in the body was normal.

Upon close questioning of the night nurses and the supervisor on duty in the nursery, it was found that the baby was not handled from the 10:00 P.M. feeding until it was taken up in the early morning. The baby had not been dropped nor roughly handled, and there were no signs of external trauma nor any discoloration anywhere on the body. No hematoma was found on the leg, nor any evidence of hemorrhage or violence.

The leg was then placed over the abdomen and chest, and bandaged in position. At the end of fourteen days, union had taken place, as noted by x-ray, so that the leg was removed from its restriction. The fracture occurred on June 29, and the last x-ray, Fig. 2, taken in September, 1936, shows the leg to be in accurate alignment.

The mother of this baby was given 60 gr. of calcium daily throughout the pregnancy and the nursing period. She also had vitamin A, B, D capsules. There was no evidence that the intake of calcium was insufficient for herself and the baby. According to the dentist's report, her teeth remained in good condition.

On checking the literature, I was unable to find anything that had a direct bearing on the case, except that in 1933 Dr. Bercovici reported a case somewhat similar. A brief abstract follows:

"It was a case of double fracture of both femurs. The x-ray showed an oblique fracture situated at the junction of the middle and upper thirds of each femur. The bones seemed to be more permeable to the rays. There was no injury which could have caused the fracture of these bones."

There is no family history of fractures in Bercovici's report, nor is there in mine. Bercovici reports 5 other cases in abstract. In 2 of these, fractured femurs occurred at the time of birth, and a few days later, fracture of the arm occurred. In 3 cases the fractures were noticed after the child was two or more years of age. In these cases it is evident that the children were suffering from "Lobstein's disease." In 1833, Lobstein described the condition by characterizing it as "an idiopathic form of brittle bones without demonstrable local lesions." Eddowes, in 1900, published a paper calling attention "to the peculiar blue sclerotics appearing synchronously with the bone lesions, and suggesting that they hold a place of importance in the symptom complex of osteopsathryosis."

The baby in our case had no evidence of Lobstein's disease.

In the Chicago area I was able to locate another patient who had multiple spontaneous fractures occurring after birth. The fractures also occurred on different days. This case is to be reported.

NEW MODEL HEAD STETHOSCOPE

AUGUST F. DARO, M.D., CHICAGO, ILL.

(From the Department of Obstetrics, Cook County Hospital)

TWENTY years ago Hillis[1] introduced for the first time the head stethoscope. The purpose of this instrument was to hear plainly the fetal heart tones and to facilitate their counting during labor without the aid of an assistant and without contaminating the sterile gloves and gown. A few months later DeLee[2] introduced

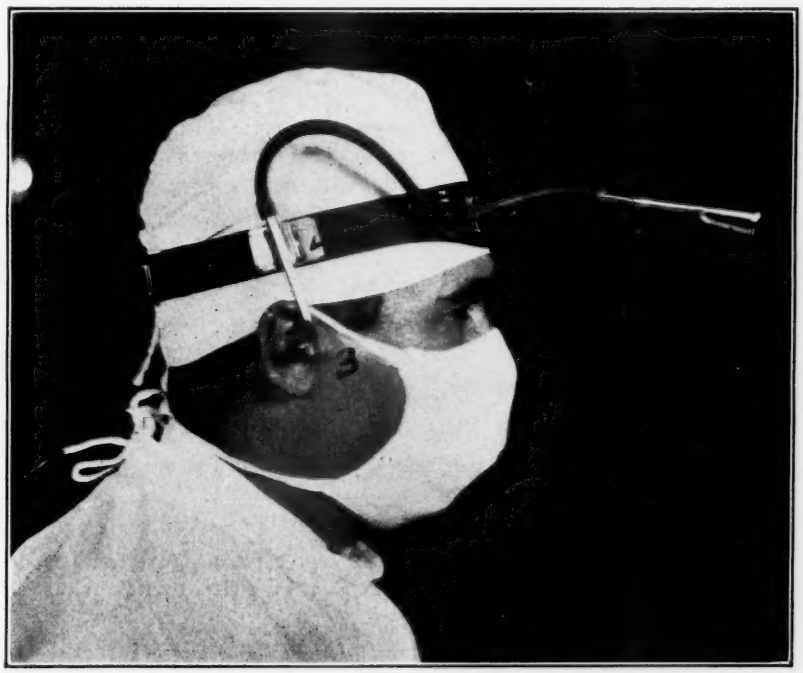

Fig. 1.—*1*, Bell stem which is two and one-half inches longer than old type. *2*, Thumb screw for flexion or deflexion of bell stem. *3*, Ear piece. *4*, Attachment for ear piece by universal joint, allowing the following movements, upward, downward, forward, backward, inward, and outward. The inward and outward movements are controlled by a simple spring which causes the ear tips to snugly fit the ears. *5*, Clamp for adjustability of headband, with special control. *6*, Clamp to keep tubing above the line of vision.

a head stethoscope with minor changes. In 1922, Falls and Hunter[3] added a watch and mirror to the stethoscope, a feature that aided in accurately counting the fetal heart tones. In 1923, Falls and Rockwood[4] designed the microphonic stethoscope amplifying the fetal heart tones sufficiently to be heard by the unaided ear a few feet from the loud speaker.

If the head stethoscope fits the head and ears it is an invaluable instrument during labor and particularly during the latter part of the second stage. An ill-fitting stethoscope is an annoyance and cannot be used with comfort or success. It is of greatest importance that the fetal heart tones be observed not only during the latter

part of pregnancy, but from the beginning of labor to the end of the second stage. Schluter[5] clearly emphasizes that the fetal heart tones be observed after each pain during the latter part of the second stage of labor. This should save more babies.

The old type of the head stethoscope is not more generally used, partly because of the failure of any one instrument to properly fit all heads and ears. I have designed a new model which is so adaptable that it will fit any wearer, thus eliminating the only objection to the instrument as a part of the equipment of the delivery room. It is hoped that the new model will facilitate and encourage the general use of the head stethoscope in obstetrics, including home as well as hospital deliveries. This stethoscope, which has been satisfactorily employed at the Prenatal Clinic and birth rooms of the Cook County Hospital for the past year, presents the following advantages: (1) The head band is adjustable to any head. (2) The ear pieces are adjustable to fit all ears. (3) This stethoscope may be worn comfortably for hours. (4) Fetal heart tones can be heard through only one ear piece, if desired. (5) The bell may be sterilized with the same solution as used on the skin. (6) It offers a clear field of vision since the rubber tubing is elevated to the head band. (7) As the rubber tubing is elevated and approximated to the bell stem, it reduces the possibilities of contaminating the sterile field when listening to heart tones. (8) During a forceps operation the long bell stem may be flexed temporarily upward out of the way. (9) Because of the thumbscrew-operated joint at the base of the bell stem, the stem may be easily adjusted to a more favorable angle.

I gratefully acknowledge the suggestions and cooperation of Dr. David S. Hillis in the designing of this instrument.

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30 North Michigan Avenue

Bager, B.: Is the Sedimentation Reaction of Any Practical Importance in Complications During the Puerperium? Acta obst. et gynec. Scandinav. **16**: 387, 1936.

The author investigated Fahraeus' sedimentation reaction in 401 women immediately before and one week after delivery with a view to finding out whether this reaction is of any value for estimating complications arising during the puerperium. About half the number of cases were normal and the other half were pathologic. The physiologic variations in the sedimentation reaction proved to be exceedingly great and capricious, both as regards the value obtained before delivery and its increase or decrease during the puerperium. Among the pathologic cases the sedimentation reaction was also shown to vary considerably. The author concludes that the sedimentation reaction is practically of no value during the first week of the puerperium even with a control value immediately before delivery for comparison.

J. P. Greenhill.

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

PSYCHOSES COMPLICATING CHILDBEARING

PHILIP PIKER, M.D., CINCINNATI, OHIO
(From the Department of Psychiatry, University of Cincinnati College of Medicine)

THE incidence of psychoses associated with childbearing has been given by various writers on the subject as ranging from 1 in 400 to 1 in 1,192. The average of the different ratios cited for Queen Charlotte's Hospital, the Rotunda Hospital in Dublin, Ireland generally, and listed by DeForest, Langdon, Frumkes, Armstrong-Jones, and Partridge is 1 in 858. In other words, of every 858 women who enter the cycle of reproduction, one is likely to become psychotic during the period beginning with conception and ending with lactation. On first thought one might be inclined to dismiss this ratio as being so small as to depict a possibility which need cause little concern. After all, a percentage incidence of slightly more than 0.1 per cent is hardly great enough to merit consideration!

We will, nevertheless, pause for a moment of consideration. In the first place these figures represent, for the most part, only those patients who are sufficiently abnormal mentally to have been noticed by the non-psychiatric observer. In the second place, a good many of the so-called psychotic developments of pregnancy do not manifest themselves until some time after delivery, so that the connection may not be recognized. As a result of these two factors, many of the less spectacular mental states and a number of those which develop postpartum probably do not contribute to the ratio I have given. Consequently, the percentage incidence probably may be assumed to be higher than 0.1 per cent.

Let us view the situation from a somewhat different angle. Cole says that 7.5 per cent of all female psychoses are associated with reproduction. DeLee places the figure at 10 to 18 per cent. The State of New York attributes 3 or 4 per cent of its total female state hospital admissions to childbearing. Zilboorg reports that of 10,000 psychotic women, the psychoses were incidental to pregnancy and its sequelae in 8.7 per cent. Stone and Karnosh found a similar association in 5.5 per cent of 1,604 psychotic women. If we roughly average these percentages, we obtain a result of 8.9 per cent. It may be said, then, that of all females who suffer from psychoses of various sorts, almost 9 per cent develop their mental disorders in connection with the reproductive experience. That 9 per cent, it seems to me, places a problem squarely in the laps of obstetricians. Since an appreciable proportion of the psychotic female population develops its mental disturbances while under the observation of the

obstetrician, he owes it to his patients and to the cause of medical progress generally to examine this problem carefully, and to take whatever steps he can toward diminishing its seriousness.

It is hardly necessary here to spend time on the phrase "psychosis of pregnancy." Obstetricians and psychiatrists alike, throughout the literature, have pointed out that there is no circumscribed mental picture that may be ascribed to reproduction. The old notion that pregnancy provides a specific etiologic agent in the production of mental disease has, I believe, been laid by the heels. It will suffice to say that the psychoses associated with reproduction appear in all of the temporal phases of the reproductive cycle, that the clinical pictures may simulate practically any of the psychoses found in nonpregnant women, and that the prognosis varies also. There is, then, no "psychosis of pregnancy." But when we recall the 9 per cent contribution of pregnancy to the total psychoses in females, and in the light of the fact that the incidence of psychoses among pregnant women is almost twice that among the female population generally, we cannot but feel that pregnancy and its implications may provide distorting influences that are more intense than women are ordinarily called upon to face. But inevitably, the question arises: why do not added stresses and strains affect all women alike? The endocrinologic, metabolic, and cardiovascular alterations of pregnancy have come to be looked upon as physiologic. Why, then, do some react to them differently than do others? The conscious notions regarding the ordeals of pregnancy and the rearing of children are, for the most part, fairly well standardized. Why should the gross emotional response of one woman to this situation vary so markedly from that of her neighbor?

The answer to these questions often is difficult to find in any specific case. When one examines the problem generally, however, the explanation is more apparent. If you will permit me to digress somewhat for a moment, I will summarize briefly the pluralistic approach to psychiatric problems. We may consider the individual, for purposes of this discussion, as having been in the beginning a mass of formless but malleable clay. What, then, were the influences which molded her into this finished product with which we, as physicians, have to deal? How did she evolve into this person with her particular physical set-up and personality? A detailed exposition of the phenomena involved would necessitate an entire series of lectures. We can, however, briefly classify the molding forces into four crude groups.

There are, first, the constitutional factors which result in the individual's native endowment, and which are derived from hereditary, intrauterine, and infantile physical influences. Next may be mentioned the factors which make for personality development—early environment and experiences plus training—which establish the emotional pattern of the individual and set up potential reactions, both desirable and otherwise, that may manifest themselves at any time during the life span, depending on the circumstances in which the individual finds herself. Third are the physical inroads of disease which may occur at any time, and which may alter the individual's capacity for adjustment either by direct action on one or the other of her tissues and organs, or by limiting or distorting her perspective and thereby making for emotional changes. The fourth, but by no means least important, group of stresses and strains are those incident to the attaining of maturity, which necessitates an assumption of

independence, an acceptance of responsibilities, an active participation in a competitive existence, and so on.

These are the forces, past and present, which determine the individual's ability to adjust, and which color the mental picture that she presents. Each force, in itself, is made up of a complexity of possible factors; and the interaction of all of them in different individuals may make for a diversity of personalities and reactions which is only to be compared to the total number of individuals existent. When, in attempting to understand the dynamics of a given mental picture, we take into account all of these factors, we are employing the pluralistic approach. There is no other intelligent manner of handling psychiatric problems—or, for that matter, medical problems generally. We must consider always the total picture that the patient presents, and resist the temptation to relax into the error of dealing with a pathologic finding as though it were a thing apart from the remainder of the individual. The psychobiologic unit that we call man always includes, is dependent upon, and reacts as a unit to all of its functions, normal and otherwise.

Pregnancy, involution, and lactation are usually regarded as physiologic processes. The facts that women are predisposed structurally to these phenomena, and that they are reared in an environment which tends to condition them psychologically to accept maternity as a matter of course, would seem to remove the stigma of pathology from the picture. In the larger biologic sense, also, the perpetuation of the species could hardly be called pathologic. And the apparent truth that the vast majority of women reproduce without mishap attests to the normalcy of the entire affair. Despite these facts, however, we must not forget that pregnancy and its sequelae do bring about profound, even though transient, physical and chemical changes in the individual. And in addition, the mental experience of childbearing and its multitude of possible emotional ramifications is hardly to be regarded as negligible. We have in reproduction, then, the superimposition on the woman of stresses which, even though they may be considered part of her physiologic and psychologic heritage, are nevertheless representative of a load that is greater than she is accustomed to carrying. When we add to this the increased possibilities for actual physical disturbance, infection, hemorrhage, thrombosis, and so on, the possible load becomes even heavier. Thinking pluralistically, we should not be surprised if some of the many possible weak links in the personality occasionally break under these added strains. It is true that there is no "psychosis of pregnancy." But pregnancy may well provide, in a variety of ways, the precipitant that will crystallize an existing potential departure from the normal.

The answer, then, to the question, "Why do some women react differently to the experience of reproduction than do others?" is apparent. Not all women are alike, either physically or in regard to personality makeup. I realize, of course, that this is no startling disclosure, and that all of you are aware of it. What is surprising, however, is the ease with which this more or less obvious fact is forgotten or neglected. The problem of the psychoses that develop in association with pregnancy is, from the practical point of view, no more a matter for purely specialized psychiatric solution than are cardiac deliria or disturbances in mental equilibrium secondary to nutritional deficiencies. The obstetrician who limits himself to an urinalysis prenatally, the delivery of the infant, and the removal of an episiotomy suture postnatally, might have spared himself

the time and expense involved in the lengthy preparation for his work. A six months' apprenticeship in an active maternity hospital would have equipped him adequately for the mechanical performance of his duties. Fortunately, however, most obstetricians are assuming the responsibilities that are properly theirs as physicians. Their interest is no longer focused exclusively on the pelvis, with the result that the metabolic and endocrinologic activities during reproduction are becoming progressively more understandable to all of us. Their consideration of the emotional implications of pregnancy, however, has not kept pace with these other advances. It is necessary that obstetrics include in its armamentarium a greater measure of psychiatric understanding. Therein rests a large part of the prophylaxis against not only the psychoses, but also the much more frequent, less intense emotional disturbances that evolve from pregnancy.

Reviewing the available English literature on the subject which has appeared during approximately the past twenty-five years, a total of 946 cases was found. It is to be regretted that the facts regarding these cases that were selected for tabulation were not discoverable in every instance. The accumulated results, nevertheless, may have some instructive value.

The literature conforms, for the most part, to the custom of classifying the types of psychoses which are associated with pregnancy into three major divisions: schizophrenic, manic-depressive, and toxic-exhaustive. Though the clinical pictures seen frequently are likely to be more or less atypical, this classification is in the main acceptable, and is particularly useful from the point of view of prognosis. In addition, most writers on the subject attempt to group their cases on the basis of the phase of the reproductive cycle in which the psychosis first was apparent. Robinson, as a result of a questionnaire submitted to a number of psychiatrists, found the consensus of opinion to be that the temporal divisions are three: the period of pregnancy, the puerperium (including the first six weeks postpartum), and the lactation period (after the sixth week postpartum). Zilboorg, in this connection, states that 15 per cent of the cases occur during pregnancy, 25 per cent during lactation, and 60 per cent during the puerperium. In our own survey, which included 770 cases concerning which this information was available, 24 per cent occurred during pregnancy and 76 per cent had their onset postpartum. Of the postpartum cases, the psychoses began within the first two weeks in 80 per cent, with lactation period contributing only 4 per cent. Precise information regarding the time of onset in the pregnancy cases was listed in only 22 instances, of which 16 occurred in the third trimester. This corresponds to the generally advanced statement that of those psychoses which begin during pregnancy, the majority first become manifest in the later months.

Concerning the diagnostic incidence, it was not possible in this survey to obtain an adequate differentiation between the schizophrenic and manic-depressive cases; so that our classification includes both of these groups under the functional division, and compares them as a unit to the toxic-exhaustive cases. The latter are reported variously as comprising 32 per cent to 48 per cent of the total psychoses. Of 891 cases in our survey, 35 per cent were toxic-exhaustive and 65 per cent functional. It is felt generally that the percentage of functional psychoses is likely to be higher among the prenatal cases than among those developing postnatally; whereas the toxic-exhaustive incidence climbs postpartum.

Of 808 cases, 60 per cent were multiparae and 40 per cent primiparae. Most statistics agree that multiparae show a greater total of psychoses than do primiparae; and the deduction that is usually drawn from these figures is that any given multipara pregnancy is more likely to be complicated by a psychosis than is a first reproductive experience. Indeed, psychologic reasons why this should be so have been advanced. I would like to point out merely that there are more multipara than primipara pregnancies; and that this fact alone may well provide the explanation for the greater number of multipara psychotics. As a matter of fact, it would not be surprising if complete data would show that the percentage incidence of psychoses is actually higher in primipara pregnancies. The unusual physiologic changes, the alterations in physical appearance, the anticipation of the ordeals of parturition, the magnification of the responsibilities of maternity generally, and the crystallization of unconscious emotional potentialities all probably contribute to making the first experience an especially difficult one mentally. In this connection, one probability worth mentioning is that psychoses seem more likely to develop during pregnancy in primiparae, and postpartum in multiparae.

It is impossible, without more data than were available, to draw any significant conclusions from the age incidence of this series of cases. The average age was thirty years, with 46 per cent occurring between the ages of thirty-one and thirty-five, and the group from twenty-six to thirty years contributing 32 per cent. A large majority of the psychoses, then, developed between the ages of twenty-six and thirty-five; but this span corresponds to the period of greatest fecundity, which dilutes the significance of the finding.

Regarding the presence or absence in the patients' histories of psychotic episodes previous to the pregnancy under observation, positive information was recorded in only 196 cases, with 81 having had psychoses with previous pregnancies, 40 not associated with pregnancy, and 75 concerning whom no mention was made as to whether or not the psychoses were coincident with reproduction. Taken as a group, these 196 comprise 20 per cent of the total; and if we assume that the actual incidence of previous psychoses would be even higher with adequate data regarding all the cases, this factor presents itself as a probably significant premonitory warning. This statement is qualified because no figures on the past histories of a control group of uncomplicated pregnancies are at hand.

An attempt to discover pertinent material regarding the prepsychotic personalities of these cases was disappointingly unproductive. Zilboorg asserts that aloofness, frigidity, chronic masturbation, homosexual trends of more than ordinary intensity, and long courtship are frequent findings in the histories, particularly of those individuals who develop the schizophrenic type of reaction. Bernard Glueck agrees with Zilboorg, and adds as predisposing qualities the schizoid personality make-up, eccentric or extremist notions regarding sexual matters in any direction, and difficulty in sharing one's self between parents and husband. Anderson, comparing these factors in psychoses associated with pregnancy to those independent of reproduction, found no significant difference in the two groups. It seems plausible that the findings of Glueck and Zilboorg hold potentialities for psychopathology regardless of whether the precipitating strain be pregnancy or something else overly strenuous physically or emotionally. Davidson does not feel that frigidity is a particularly decisive force in the causation of the psychoses under discussion.

Strecker and Ebaugh found in their material some suggestion that Jewish women are more susceptible to severe mental upset as a concomitant of the childbearing experience than are women of the other religious groups. I was not able to find any other data or opinions concerning the existence of racial or religious differences in this matter. McGoogan stresses the importance, as predisposing factors, of previous pregnancy experiences and of heredity. Crowder feels that hypo-ovarianism holds grave prognostic possibilities.

Regarding the significance of the presence of hereditary taint, the literature covered by this survey was again inadequate. Reference to the presence or absence of markedly abnormal mental findings in the ancestries of these cases was not made in a large number. From those reports which included this information, 163 cases with definite pathology in the family tree were found. Considered against the background of the total number, these make up 17 per cent. It is quite probable that with complete historical information in every instance, this percentage would be appreciably higher. Despite the fact that this degree of incidence of hereditary findings is significant statistically, the usual difficulties encountered in trying to evaluate hereditary influences generally are present here also. Perhaps the most honest attitude would be to view a patient's poor heredity with suspicion, but to avoid allowing it in itself to play too prominent a part in the coloring of predictions regarding the course in any given case.

A possible contributing circumstance that has been given a good deal of consideration is illegitimacy. The additional affective stress that is the usual complement of illegitimacy, plus the probability that illegitimate pregnancies are more likely to occur in women who are, to begin with, less well-adjusted emotionally, intellectually, and financially, would seem to make it likely that this unconventional factor identifies a group which has a greater chance of becoming psychotic during the reproductive period than have more conforming women. Partridge states flatly that the percentage incidence of psychoses associated with illegitimate pregnancies is greater than one finds in married cases. Armstrong-Jones says that of all the cases he could find, 12 per cent were illegitimate. The latter compares this figure to the smaller total incidence of illegitimate births in the population generally, and deduces that the discrepancy can only mean that illegitimacy is a definite factor in the production of psychoses. He points out, also, that most of the psychoses in these cases occur before delivery. This, from the purely psychogenic point of view, should not be difficult to understand; and in addition, the comparatively high incidence of psychoses among illegitimate cases should eliminate any doubt that might exist regarding the ability of psychogenic factors to produce mental upheavals.

The problem of infanticide has earned some comment in the literature. Rieksher says that it is rare. Hopwood found that of all murders committed by female psychotics generally, 25 per cent were instances of infanticide. He states that these crimes occurred for the most part during the lactation period. McIlroy, investigating statistics at the Criminal Lunatic Asylum at Broadmoor for the period from 1900 to 1924, found that 42.8 per cent of the admissions were for child murders in connection with psychoses associated with pregnancy. She, too, points out the higher incidence during lactation, and is inclined to blame the psychoses

on the occurrence of physical and mental exhaustion in undernourished and overworked women. According to McIlroy, depressions are more frequent than excitements in the lactation period. With the patient farther removed from parturition, and consequently more likely to have discontinued medical care; and with the depression not so likely to stimulate close observation on the part of the family as is the more spectacular excitement of the earlier psychosis, the opportunities for infanticide are accordingly enhanced. It would be well to point out at this time also that inadequate observation likewise increases the chances for suicide in these patients, as it does in all mental cases. Despite the tendency in some quarters to consider child-murder a rarity, Langdon's feeling that every psychotic woman who has a child should be considered potentially infanticidal merits judicious incorporation into the attitude of the physician who handles such a case. Certainly with this attitude the chances for infanticide will be diminished. The reminder by Morton, who points out that not every infanticide is an indication of insanity, should be remembered, particularly when the legal aspects of these cases are being considered.

Concerning the outlook in the cases under discussion, it is generally agreed that the prognosis may be considered good in most instances. Figures given by various clinicians range from 76 per cent to 53 per cent recoveries. Of 719 cases in this survey (deaths not included) concerning whom the outcome could be determined, 65 per cent terminated favorably. It is well to keep in mind that a large proportion of these cases were state hospital patients, and therefore could be assumed to represent the least favorable prognostically. The outlook, consequently, probably may be considered even more optimistic than these figures indicate. Of 283 recovered cases in which the duration of the disease was determinable, the psychosis lasted less than one month in five, from one to three months in 49, from three to six months in 110, from six to twelve months in 81, and more than a year in 38. Thirteen patients remained psychotic for approximately eight years each, and then recovered. If these 13, who distort the total picture unduly, are eliminated, the average duration of the psychosis in these 283 cases was six months. It was not possible in this survey to attempt an estimate of the prognosis in the light of the time of onset of the psychoses. It is probable, however, that predictability in cases of this sort is more properly dependent on the type of mental reaction that occurs than it is on the time of occurrence. In this connection, James says that 96 to 97 per cent of the manic-depressive cases may be expected to recover from any given attack, with recurrences, of course, quite possible; that the outlook in the toxic cases is excellent if the physical pathology can be overcome; and that the schizophrenic types offer the worst prognosis. He points out that even though the psychosis persists for as long as a year, recovery may still take place. Even though the schizophrenic reactions present the least favorable possibilities, the prognosis in these cases should be considered definitely better than in schizophrenia generally. Concerning the time of occurrence some writers have felt that, with regard to the postpartum cases, the seriousness of the prognosis increases with the lengthening of the interval between delivery and the onset of the psychosis.

There exists in many quarters something akin to a superstition that psychoses occurring during pregnancy are likely to disappear with mi-

raculous suddenness at the time the uterus empties itself. Except for an occasional toxic case, where the toxicity apparently is dependent specifically on the pregnant state, the regression of the mental abnormalities usually may be expected to be gradual. The intervention of death in these patients is more properly a function of the physical than the mental condition; though in the toxic cases particularly, the superimposition of exhaustion secondary to excitement or malnutrition is likely, of course, to accentuate the gravity of whatever somatic disorder may be present. It is in the toxic group that most of the fatalities occur. Regarding the mortality among the children born to women who are psychotic during pregnancy itself, Rieksher finds the rate to be high. To recapitulate briefly, then, the prognosis generally may be considered good, even in psychoses of relatively long duration. This is especially true among those women whose prepsychotic personalities and adjustments were adequate.

Wherein, now, may the obstetrician look for possible danger signals in his patients? Some of the more frequently occurring immediate premonitory manifestations are evidences of general discontent on the part of the patient, emotional changes in the direction of either depression or excitement, increasing tension, excessive anxiety, apprehension, and agitation. The introduction into the picture of marked irritability, suspiciousness, the development of phobias, and personality changes generally should cause the physician to be on his guard. Insomnia is often an ominous sign, as is the development of physical exhaustion. Fairly frequently the first sign of an oncoming mental upheaval is a newly developed concern over trivialities; and increasing garrulousness is felt by some authors to be particularly significant.

In addition there are the more remote, but nevertheless important, factors which always bear investigation from the point of view of anticipating a mental break. First and foremost, of course, are the general physical condition of the patient, and her physiologic ability to withstand the rigors of reproduction. The course of the pregnancy, the severity of the labor, and the efficiency of the involution and other postpartum phenomena hold possibilities for upset. The expectant mother's observable emotional reaction to childbearing and its various implications merits consideration. It is important to discover, if possible, how apprehensive she is regarding pain, and how courageous she usually is in the face of discomfort. The existence of a schizoid personality, and particularly the history of previous "nervous breakdowns" are warnings that should not be neglected. Unsuccessful attempts at abortion, in addition to the possible physical sequelae, frequently result in conscious and unconscious guilt feelings that may play havoc with the patient subsequently. The factor of illegitimacy may be disturbing. The general characteristics of the patient's environment and her attitude toward it, her adjustment to her husband and his reaction to her pregnancy, her degree of emotional maturity, her intellectual capacity, the economic problems that she must face because of the expansion of her family—all these details, and more, need to be considered in estimating the patient's mental capacity for adjustment to the various stresses of reproduction.

The obstetrician, if he is to do his patient justice, must bear all these things in mind. It is not nearly enough to become thoroughly acquainted with the pelvic outlet. He, in common with all physicians, must view

his patient as a psychobiologic unit, the different constituents of which are intimately interrelated, the cardiac efficiency with the intrauterine nutrition, the endocrine activity with the circulatory tension, the psyche with the soma. Not only the major psychoses, but also the less intense maladjustments which may make for a much greater total of unhappiness, might well be avoided in large part if more obstetricians interested themselves in the complete personal and physical lives, past and present, of their patients. Whether, as Bernard Glueck has put it, the patient is possessed of psychobiologic fitness for marriage should be of primary concern; knowing this involves, of course, an expenditure of time, frequently, considerable time. The patient has a right to expect this sort of interest from her doctor. If his conscience does not force him to investigate his cases from every angle, and to measure emotional potentialities and repair mental trauma as he does pelvic diameters and perineal tears, he is only half a physician. The psychiatrist can help, of course. In the majority of cases, however, properly interested management on the part of the obstetrician will eliminate the need for specialized psychiatric aid.

There has been a definite effort made, during the past decade especially, to anticipate mental and emotional difficulties through an alliance between pediatricians and psychiatrists. It seems to me that we might well begin our prophylactic approach at an even earlier developmental level. If we want well-adjusted children, we must strive for emotionally efficient motherhood. To the obstetrician is given the opportunity for preparing the way.

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Editorial

The Physician as Practical Eugenist

AS POPULATION experts elucidate the statistical intricacies of the differential birth rate, and while the biologists pile up the evidence of gene responsibility for many of the excellencies and inferiorities of mankind, the general public is beginning to lose its traditional confidence in haphazard breeding of children.

The physician finds himself very much "on the spot." He is again as on many previous occasions of his long travel from individual towards social medicine, at a sort of crossroads with the professional sign board giving him equivocal directions.

Shall he keep to his original job of treating the sick and leave to the sociologist, the journalist, the geneticist, the promoter of general welfare at large, to translate into public understanding and personal conduct the lessons of human biology?

Shall he shoulder a new undertaking and prove that he is practically as well as etymologically a *Doctor?*

It would be contrary to good precedent and an evidence of professional retrogression if the physician of today did not meet the challenge of the instant need with the courage bred of knowledge.

Such resources as society can control will inadvertently, or, with good or evil intent, be used to impair or improve the physical and mental qualities of future generations. It is the study of such agencies, such forces and tendencies of society which constitutes eugenics.

In this the physician has an ever deepening concern and cannot long escape a professional decision as to his overt action in the matter of particular families or prospective parents, or of the premarital couples who must or wish to seek his aid in an intelligent way of married life.

The questions may be as blunt as "To marry or not," "If marriage, then what?", "Shall we have children, and probably what kind?", "Will you help me, or us, to mate and so breed as to offend neither the offspring, nor the society of our time and later?"

What the physician can contribute is perhaps little in amount, but in quality big with potentialities. He can reach another and more critical level of interest on his spiral stairway of preventive medicine. Having established the necessity and value of prenatal care he pushes back the threshold of his concern into the preconceptive choice of marriage conduct, and further still into the elements of choice that may prevent or determine marriage.

* * *

The physician must always consider himself the direct inheritor and personal employer of all sound biologic knowledge for human ends. He

will receive, and as a student of medicine should demand, an increasing breadth of instruction on the social and individual implication of eugenics. As he takes his clinical histories he will surely be more than ever inquisitive as to the factors of inheritance.

He will encourage the requirement of premarital medical review of prospective parents, more for avoiding genetic than syphilitic catastrophes. He will inform himself on, and share with his patients, the safe techniques which may spare the parents humiliation and the inevitable sorrows of mismating.

He will teach the precious privilege and high degree of safety of normal maternity for the wholly fit.

He will take part in efforts for reversal of dysgenic tendencies which threaten to wreck nations as well as the family, by learning and then practicing eugenics through teaching the principles of racial progress.

Haven Emerson, M.D.

Correspondence

Gas and Air Analgesia

To the Editor:

In this country we are greatly indebted to American anesthetists for their pioneer work in analgesia and anesthesia in labor, and the article in the November number of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY by Dr. Arthur Bill is of great importance. Anesthetists will be envious of the splendid results obtained.

Dr. Bill mentions the bitter opposition to proposals for the relief of pain which is still not altogether uncommon and I think that, with us, this opposition arises for three reasons. (1) Many practitioners fear that the general demand of analgesia in labor will greatly add to their work and their difficulties; (2) the bad results obtained, as Dr. Bill says, due to bad judgment or bad technique; and (3) the bad results obtained from an attempt to conduct every labor entirely painlessly.

Many practitioners believe that if there is a general demand from women for relief from the pains of childbirth, they will be called upon to spend many hours at the bedside of their patients administering an anesthetic, and there is a very real fear on the part of the overanxious practitioner that the administration of analgesia and anesthesia in labor often leads to premature interference with the normal process of labor, and it may have a bad effect on both mother and child.

This fear is not entirely groundless, because there is evidence today that, in an attempt to produce absolutely painless labor, we can kill by kindness.

In his article, Dr. Bill brings out very clearly what are the general difficulties standing in the way of any attempt to relieve all the pains of labor for all women. "Clever administration of the general anesthetic is really the most important part of the conduct of painless labor," he says; and we all know how few in number are the clever administrators. In conclusion, he tells us it must be assumed that for conducting the type of labor described by himself, there must be adequate facilities, so often found only in hospitals. In the discussion which followed Dr. Bill's paper, other practitioners bring out the same difficulties.

These are just the difficulties with which we have been faced in this country for many years. Here, about one-half of the total confinements are conducted by midwives in the patients' own homes without the presence of a doctor. Of the remainder,

about 300,000 cases a year, some go to hospitals where expert obstetric anesthetists are not provided, others are attended in their own homes, or in nursing homes by the general practitioner (and our nursing homes sometimes leave much to be desired). Only a very small proportion, one might say a negligible proportion, of women in England are attended by a skilled obstetrician accompanied by a skilled anesthetist.

At one time the difficulties indeed seemed insurmountable and would have been insurmountable, had it not been for the unremitting efforts of a body of lay people led by Lady Baldwin and Lady Rhys Williams, who formed "The National Birthday Trust Fund" to provide money so that research work might be done in order to find some way by which all women could be given at least some relief in their labors. A start was made with chloroform in the form of chloroform capsules. These chloroform capsules are small crushable glass ampoules containing 20 minims of chloroform, and are crushed and placed in a mask which is held two inches from the patient's face when in pain.

Very good results were obtained and permission was sought from the appropriate authorities for their general use.

The British College of Obstetrics and Gynaecology carried out a test of chloroform administered by various methods to see whether the required permission ought to be granted, but they came to the conclusion, with considerable regret they said, that in considering the results of chloroform analgesia the conclusion was reached: that the administration of chloroform in any form or by any method carried with it a danger of death.

It was evident then that chloroform is not the agent for which we so earnestly sought.

Nitrous oxide and oxygen was considered impracticable because it was thought that that apparatus was too expensive for everyday use, too difficult to carry about, and that its administration could not be placed in the hands of midwives.

In 1933, however, a great advance was made. Dr. Minnitt, an anesthetist of Liverpool, suggested using a mixture of nitrous oxide in air instead of nitrous oxide and oxygen, of such strength that from its inhalation, no patient would be fully anesthetized. Dr. Minnitt found that when nitrous oxide was inhaled, a period of insensitiveness to pain was experienced before consciousness was lost, and he described this condition as analgesia.

He used an automatic apparatus for the administration so that all the patient had to do was to breathe in and out from a rubber facepiece, laying the facepiece on one side when the pain passed away, and the flow of gas was automatically shut off.

Dr. Minnitt's method was taken up enthusiastically by the "National Birthday Trust Fund" which paid all expenses for an official investigation of his technique by the British College of Obstetrics and Gynaecology. The College came to the conclusion that the administration of gas and air by the Minnitt apparatus was not associated with any increase in the risk of death in childbirth, that the method did not involve any added risk to the fetus, that the actual administration did not call for any more special skill than that which might be required by a midwife during her period of training, and that relief from pain was obtained in a high percentage of cases.

They also found that the administration of gas and air carried with it no remote risk to the baby, and that the method had no deterrent influence on the natural course of labor.

The Central Midwives Board have now altered their regulations to enable midwives to administer gas and air analgesia to their own patients.

At the Wellhouse Hospital, Barnet, and at the British Hospital for Mothers and Babies, Woolwich, we have used gas and air analgesia for all our cases and are well satisfied with the results. We do not obtain painless labor because we do not start our administration of gas and air until there is some prospect of delivery taking place, and we make no attempt to render the patient unconscious.

For primiparas, we usually start the administration when the cervix is nearly fully dilated, and for multiparas, when the cervix is dilated to the size of a 5

shilling piece. There are two reasons for this. First, *cost:* Nitrous oxide gas in this country costs 5 shillings per 100 gallons, and our average cost has worked out at 2/6 per case, which means that our average period of administration was one hour. In some cases the gas and air was administered for shorter periods, in others, longer.

We find the average consumption of nitrous oxide is about 50 gallons per hour, intermittent flow, and as hospital committees are always closely watching every item of expense, the cost of gas must not be very high.

Our longest case was a twenty-five-hour administration, but however long the administration lasted, no ill effects were observed.

Second, we never have quite so many nurses as we would like, and once the administration of the analgesia has been started, the patient must never be left, and it is not always practicable to keep a nurse constantly beside a patient for several hours.

We do not as a rule give sedative drugs in the early stages of labor, not because we do not believe in their use, but because we feel that after a sedative drug has been administered, the patient must be closely watched, and our staff is limited.

For my own cases in private practice, I always administer some sedative early in labor, and I find that by this means the value of the inhalation analgesia is enhanced. I usually give 1/4 gr. of morphia, but have obtained good results with sodium soneryl.

At the Wellhouse Hospital, I have recently analyzed a series of 1,500 consecutive cases and found that 541 primiparas experienced no pain whatever after the administration of gas and air was started and 331 primiparas obtained great relief, but 8 obtained no relief whatever. There were 332 multiparas who experienced no pain, 280 multiparas had great relief, and 8 were disappointed.

It will be seen then that we have obtained a high degree of success from a method which can be used for all women whatever their situation, and by whomsoever they may be attended.

In most of our municipal hospitals the conduct of a normal confinement is left in the hands of a competent midwife, and it has been shown that the midwife can take complete charge of the administration of the analgesia with conspicuous success.

In the home those who are attended by the general practitioner make use of Dr. Minnitt's method. The gas and air is nearly as much help to the doctor as to the patient. He is no longer called upon by anxious relatives to "do something" because of the patient's distress, and he need not be present during the administration of the analgesia, but can be sent for by the nurse when his presence is required.

Steps are now being taken to arrange that all those patients who are attended by midwives in their own homes, without the presence of a doctor, shall have the advantages which gas and air can give.

It was felt that the principal difficulty in the way of a general adoption of gas and air analgesia was that midwives could not be expected to carry heavy gas cylinders and bulky or expensive apparatus, but two new easily portable machines have recently been produced. The whole apparatus (Fig. 1), gas cylinder, and all fits into a small case and can easily be carried on a midwife's bicycle or in the doctor's car without any inconvenience.

I cannot help feeling that there must be an opening for this gas and air technique in the United States, because there must be many areas where no hospital facilities are readily available, and I believe, as in this country, that the great majority of women are delivered in their own homes.

We do not claim that gas and air gives absolute relief from all pain, but in the great majority of cases, labor is robbed of its terrors.

It has been argued that there is no technique of administration of gas and air, but I regard the technique as extremely important, and I find that the degree of success obtained from gas and air depends on the amount of trouble taken by the attendant. Attention must be paid to small details. Care must be taken to see that the apparatus is in order, that the cylinders contain gas, and that the gas is turned on.

The patient should clearly understand exactly what to expect, she must be told that she will not lose all sense of consciousness and that she will not lose all sense of feeling. She must be persuaded to cooperate, and here we realize the importance of not making the patient too sleepy with sedatives in the early stages of labor, because the importance of the cooperation of the patient cannot be overestimated.

The patient must be told to apply the facepiece of the apparatus firmly to her face and to breathe deeply in and out as long as the pain lasts, laying the facepiece aside when the pain passes away. When she comes to the pushing down stage of labor, the patient must be told to take 4 or 5 deep breaths of gas, hold her breath and push, then 4 or 5 more deep breaths, hold her breath, and push again. When the baby is actually being born, we administer continuous gas and air, and after about 30

Fig. 1.

breaths of gas and air, patients are quite insensitive to all pain, or at least do not care whether they have pain or not.

There is some little division of opinion as to what is the best percentage of nitrous oxide in air. Dr. Minnitt advises 45 per cent nitrous oxide, but we do not consider this enough, and to all our patients we have administered 60 per cent nitrous oxide in air. We have seen no ill effects whatever resulting from this percentage and patients do not become cyanosed, and we have no difficulty with asphyxiated babies. With percentages over 60 per cent, cyanosis does occur in some cases, although some patients tolerate 70 per cent gas very well.

Gas and air will not suffice for forceps delivery, but we find that we can satisfactorily insert two or three stitches to repair a small tear of the perineum after the patient has had about 20 breaths of gas.

There are types of patients who do not benefit from gas and air analgesia. The very nervous patient, the very heavy patient, and the patient who has had previous experience of delivery under full anesthesia are sometimes dissatisfied, but these only constitute a small percentage of the total.

We do not claim by means of gas and air analgesia to give the absolute complete relief that the skilled anesthetist can give with nitrous oxide and oxygen, but we do claim that this method provides a safe and practical means of relieving pain in the second stage of labor for that vast number of women who are unable to engage a skilled anesthetist to attend them in their confinements.

John Elam, M.D.

48 Station Road,
Barnet, England

Frigyesi, J.: The Operative Treatment of Tuberculosis of the Adnexa, Monatschr. f. Geburtsh. u. Gynäk. **105:** 193, 1937.

It is now well established that tuberculosis of the female genitalia is secondary to a similar local process elsewhere in the body or to generalized tuberculosis. Frigyesi has observed 22 such cases. In 4 of them Aschheim-Zondek tests were done and in 2 the result was positive. In 5 of the 22 cases a correct diagnosis was made before operation.

The treatment has changed considerably during the last few years. Many authorities are now opposed to operation because of the high mortality and morbidity especially on account of bowel injuries. Roentgen ray therapy is followed by diminution in the size of the masses, and the symptoms subside.

Among the 17 operated patients, 7 were cured, 4 were improved, 3 were unimproved and 3 could not be traced.

The author is of the opinion that operation should be avoided. In cases of doubt a laparotomy is advisable. When conservative and general treatment fail to produce a cure, an operation may be performed with a fairly good prognosis.

J. P. Greenhill.

v. Pallos, K.: Symptomatology and Pathology of Granulosa Cell Tumors, Monatschr. f. Geburtsh. u. Gynäk. **105:** 139, 1937.

According to v. Pallos there have been recorded about 400 cases of granulosa cell tumors in the literature. He reports three cases.

It is almost universally believed at present that these tumors are histologically malignant but clinically benign. In an analysis of about 200 well-described cases, the author found that pain was present in 7.6 per cent, ascites in 8.1 per cent, loss of weight in 4 per cent, inoperability in 0.7 per cent, and recurrences in only 4.5 per cent. The incidence of recurrence in ovarian carcinomas is over 50 per cent.

It is commonly believed that the proper treatment is simple removal of the tumor. On the other hand there is a difference of opinion as to whether or not radiation therapy should be applied. v. Pallos believes that radiation therapy should not be employed because half of these tumors occur in women who are in the reproductive era and because the tumors are clinically benign. However, since we cannot tell which tumors will turn out to be clinically malignant, patients who have had granulosa cell tumors must be watched closely after operation. Bleeding will nearly always indicate a return of the growth.

J. P. Greenhill.

Department of Reviews and Abstracts

Conducted by Hugo Ehrenfest, M.D.

Selected Abstracts

Pathologic Labor

Jungman, Gerhard: New Viewpoints of the Question of Deflexion Attitudes, Ztschr. f. Geburtsh. u. Gynäk. **112:** 183, 1936.

The author concludes from his study of ten cases in which there were exaggerated deflexions of the head that the condition is entirely due to the shape of the fetal cranium. He believes that deflexion will occur when the cranium is longer than normal in the region of the occiput. The greater size of the occiput compared with the sinciput prevents it from going deep in the pelvis as it necessarily encounters more resistance.

E. S. Auer.

Jacobs, J. Bay: Persistent Occipito-Posterior—A Simple and Safe Method of Treatment with the Use of a New Forceps, South. M. J. **29:** 891, 1936.

Occipitoposterior presentation is a frequent cause of prolonged labor and dystocia. Present-day widespread use of obstetric analgesia is a definite contributing factor to the causation of this condition, since the patient's cooperation in the use of her voluntary efforts is lacking.

A large percentage of occipitoposterior rotations given enough time will rotate anteriorly spontaneously, but intervention by skilled men considerably shortens labor and yields very good results.

The author presents and describes his obstetric forceps which permit rotation of the posterior occiput and extraction with a single application. In size and appearance they resemble Tucker-McLane forceps.

The stressed advantages of the forceps are: (1) Proper cephalic application of forceps is easily made; (2) necessity for alteration of position of blades or for their reapplication is obviated and thus the head cannot rotate posteriorly; (3) it is the simplest method yet proposed for treatment of occipitoposterior rotation.

Arnold Goldberger.

Nandi, Gorachand: Habitual Breech Presentation, Calcutta M. J. **31:** 289, 1936.

A discussion is presented of the clinical phenomenon of breech presentation occurring repeatedly in the same woman. In the literature Dahlem first drew attention to this condition in 1886 when three cases were reported, two of whom had 5 children, all in breech presentations. Since then numerous cases have been reported with habitual breeches occurring from 3 to 9 times in the same woman.

The etiology is primarily the absence of those factors that lead to a cephalic presentation. Accommodation and gravity are the chief causations of head

presentation. In the majority of cases of breech an habitual condition is present. Pelvic contractions, abnormality of size and shape of the head, pathologic anomalies of the head, abnormalities in the shape of the uterus, prematurity, and hydramnios are all predisposing causes. Multiparity, twins, and fetal macerations are frequently associated with breech presentation. The hereditary and individual tendency must be recognized.

F. L. ADAIR AND S. A. PEARL.

Goethals, Thomas R.: The Risk to the Infant in Breech Delivery, Surg. Gynec. Obst. **62**: 525, 1936.

In the 1,242 breech deliveries in the Boston Lying-In Hospital during the years from 1913 to 1934, the gross combined fetal (stillbirth) and neonatal death rate was 25.7 per cent. In 272 deliveries, either the pregnancy was pathologic, with such complications as preeclamptic toxemia, eclampsia, nephritis, syphilis, diabetes, hydramnios, etc., or labor was complicated by such conditions as placenta previa, ablatio placentae, or prolapse of the cord, with a crude mortality rate of 51.8 per cent; and resulted in the birth of 43.3 per cent of premature infants, with a crude mortality rate of 82.2 per cent.

In the 970 deliveries uncomplicated by pathologic pregnancy, the crude mortality rate was 18.5 per cent; uncomplicated deliveries produced premature infants in 15.7 per cent of the cases, with a crude mortality rate of 62.1 per cent.

Placenta previa, ablatio placentae, and prolapse of the cord are respectively three, five, and five times more often associated with breech presentation than are all types of delivery.

The mortality rate was 13.6 per cent among 916 newborn infants (excluding macerated and grossly malformed babies), subdivided as follows: 53.6 per cent for premature, 10 per cent for immature, and 6.9 per cent for mature infants. This last figure represents the risk to the living, undeformed, full-term infant in utero who is destined to be born by breech delivery in the absence of pathologic pregnancy and of hemorrhage and other accidents of labor due to abnormalities of the placenta or of the umbilical cord.

WM. C. HENSKE.

Soule, S. D.: Breech Delivery, J. Missouri M. A. **33**: 449, 1936.

A series of 328 breech deliveries is reported with a combined ward-private service fetal mortality of 7.45 per cent. Traumatization is the chief cause of mortality in breech delivery. Prolonged second stage of labor, cervical dystocia and difficulty with the aftercoming head account for most of this traumatization. A "hands-off" policy is to be observed until dilatation of the cervix is complete. Spontaneous delivery of the breech is preferred if progress is steady. With a delay of longer than two hours in the second stage of labor the breech is pushed up, decomposed, and extracted. Complete breeches and footlings are delivered as soon as dilatation of the cervix is complete. Episiotomy is performed as soon as the vulva is distended. Traction on the aftercoming head is to be eliminated so far as possible. The Wigand-Martin maneuver is preferred to all other manual procedures for delivery of the aftercoming head, the abdominal hand serving to aid flexion only. If any resistance is encountered, Piper forceps are applied to the aftercoming head. The increased fetal mortality in multiparae in this series is definitely associated with fetal weight of more than 3200 gm. Breech delivery is an obstetric complication of major consequence.

J. THORNWELL WITHERSPOON.

Rosenfeld, Samuel S.: Podalic Version, Am. J. Surg. **31:** 103, 1936.

One hundred twenty babies were delivered by podalic version, employing the Potter technique. There was a real indication for version in every case. The corrected fetal mortality was 3.3 per cent, only slightly higher than in a series of normal deliveries.

Given good obstetric judgement, podalic version is an ideal procedure for the lesser degrees and in some cases even of moderate degrees of pelvic contractions or disproportions. It is also of great value in malposition such as posterior occiput, transverse and face positions. The Potter technique is the preferred method. In cases where difficulty is experienced in the delivery of the aftercoming head, forceps should be applied more often.

J. Thornwell Witherspoon.

Kelly, J. B.: Belated Transverse Presentation with Recovery in Twin Pregnancy, Brit. M. J. **1:** 311, 1936.

A case is reported of a twin pregnancy in which one fetus presented transversely and on admission to the maternity hospital had prolapsed a foot, a hand, and a loop of cord. Delivery occurred rapidly. The first born was moribund, but recovered in spite of prolonged pressure on the cord antenatally. The circulation was also restored in the prolapsed foot which had looked almost black before birth. Two placentae were present. A large blood clot was present between the two placentae.

F. L. Adair and S. A. Pearl.

Cordua, R.: Delivery of a Soft Head, Zentralbl. f. Gynäk. **60:** 2295, 1936.

Wieland (in 1908) has proved that unusual softness of the baby's skull is not due to rachitic changes but is the result of abnormal processes of apposition and resorption of otherwise normal bone tissue. There is apparently no relationship between this condition and the various disturbances of ossification such as osteogenesis imperfecta, osteopsathyrosis congenita, chondrodystrophia fetalis, etc.

Two cases came under the author's personal observation. In the first case the baby was craniotomized because all other attempts at delivery had failed. Subsequent examination revealed a widened sagittal suture with marked enlargement of both fontanels. On the slightest pressure the soft parts were seen to bulge like vesicles. In the second case the sagittal suture was also widened, both parietal bones and the occipital bone were thin and soft and there was also a spina bifida. Following an operation for the latter condition, the child died on the fourth day after delivery.

The author states that in these cases it is very difficult, if not impossible, to diagnose correctly the presentation because of the alterations of the fontanels. These heads, furthermore, are delivered spontaneously, only with great difficulty owing to the elasticity of the presenting part. Application of forceps usually leads to severe injury of the head.

Richard Somma.

Marx, A. N.: A Remarkable Case of Precipitate Labor, Med. Klin. **32:** 734, 1936.

A correct diagnosis of precipitate labor has an important bearing on forensic medicine. It is not possible to make a definite diagnosis of precipitate labor from an examination of mother and child alone. It is always best for the judge to instruct the mother to give a detailed account of the labor in her own words. In all cases of precipitate labor both mother and child run a number of risks. If the cord tears during the fall of the baby the latter may bleed to death or suffer

severe cranial and intracranial injury. The child may suffocate if measures are not taken to see that it breathes properly. Precipitate labors frequently result in expulsion of a baby into a toilet. This is usually brought about by the fact that patients in labor experience a desire of having a bowel movement. The author reports a very interesting case which had marked legal significance. In this case the child was expelled into the toilet by the patient without her knowledge. The child was subsequently found alive. The author points out many pitfalls which would have led some jurists to the erroneous impression that the mother had purposely thrown the child into the toilet.

J. P. GREENHILL.

Trillat, E.: Statistics of Postpartum Hemorrhage in 10,000 Deliveries, Bull. Soc. d'obst. et de gynéc. **25:** 247, 1936.

The author's criterion of postpartum hemorrhage is a loss of 500 c.c. or more of blood. In a series of 10,000 labors he found that 703 patients lost more than this amount, an incidence of 7 per cent. Twenty-three patients lost between 1,500 and 2,000 c.c., and 5 patients between 2,000 and 2,500 c.c. of blood. The uterus was invaded in 104 of the 703 cases. There were 10 deaths in this series representing an incidence of 1.4 per cent. Strange to say, there were no deaths among the 5 women who lost more than 2,000 c.c. of blood. There were 7 deaths among 557 women who lost between 500 and 1,000 c.c. of blood, one death among 108 women who lost between 1,000 and 1,500 c.c. of blood, and 2 deaths among 23 women who lost between 1,500 and 2,000 c.c. All the patients who died had evidences of infection.

J. P. GREENHILL.

Herold: The Treatment of Postpartum Hemorrhage With Special Consideration of the Henkel Treatment, Monatschr. f. Geburtsh. u. Gynäk. **103:** 1, 1936.

In reviewing the literature on the use of the Henkel method of stopping hemorrhage in cases of profuse postpartum bleeding, the author found reports of 200 cases. He also obtained information concerning about 300 additional cases, and with the exception of one case of a vesicovaginal fistula which Henkel himself described, no harm has resulted following the use of the Henkel procedure. The author therefore recommends the method which consists in the temporary application of a clamp through the vagina to the uterine artery on each side of the cervix. He recommends this procedure in cases of cervical lacerations, uterine atony and also of placenta previa, and premature separation of the placenta.

J. P. GREENHILL.

Cosgrove, S. A.: Obstetric Hemorrhage and Its Management, South. M. J. **29:** 1219, 1936.

Of the lethal triad, sepsis, hemorrhage, and toxemia, hemorrhage accounted for the highest number of purely obstetric causes of death in the author's experience.

Because of the seriousness of this complication it is vital to anticipate it.

The frequent association of bleeding with the toxemic states stresses the importance of careful prenatal supervision. Gravid patients must be instructed concerning the significance of bleeding and the importance of prompt report of its occurrence. Routine blood grouping of antenatal patients is desirable. Hospitals must be ready for rapid and efficient treatment of hemorrhage. The author

describes the customary treatment of obstetric hemorrhages. Measures to combat shock should take time-precedence over measures to control bleeding.

In respect to the cause of postpartum hemorrhage, routine examination of cervix and deep vagina for lacerations should be a first consideration, particularly after instrumentation. Secondary uterine atony, the next most common cause, is attributable largely to mismanagement of the third stage through neglect to observe the progress of events within the uterus and also to a desire to hasten its termination. Pure inertia uteri should be treated by pressing the lower uterine segment against the sacrum and by compression of the corpus between one hand on the abdomen and the other in the vagina. Oxytocics may be repeatedly applied. The author does not advocate packing of the uterus because it is unphysiologic and carries the risk of infection.

ARNOLD GOLDBERGER.

Carcoux: Uterine Ruptures Observed in the Hanoi Maternity from 1930 to 1934, Gynéc. et d'obst. **33**: 366, 1936.

Carcoux reviewed a series of 52 cases of uterine rupture. Not one of the patients was a primipara and only one was a secundipara. All the other patients had had from 3 to 13 children. The 3 important symptoms of this complication were hemorrhage, shock, and infection. In all of the cases the fetus was expelled into the abdominal cavity and in all the cases the placenta had separated at the time of operation. The most important factor in the death of women who died quickly was shock. In all but 2 cases the condition was treated by subtotal hysterectomy. There were 23 deaths in this series, most of them due to generalized infection or peritonitis. Two women died of secondary hemorrhage. Some authorities maintain that if the fetus is not entirely free in the abdominal cavity it should be extracted from below. The author, however, warns that this is a very dangerous procedure.

J. P. GREENHILL.

Vitamins and Pregnancy

Gaehtgens, G.: The Daily Need of Vitamin C in Pregnancy, Arch. f. Gynäk. **164**: 571, 1937.

The author carried out prolonged studies on the vitamin C needs of ten healthy pregnant women. Using the Widenbauer method, he determined the daily need of cevitamic acid to be 33 to 64 mg. Thus the daily requirement of vitamin C is not greater for the pregnant than for the nonpregnant woman. The usual deficiency found during pregnancy is probably due to the needs of the fetus and the passage of the vitamin C through the placenta. The addition of 100 mg. of vitamin C to the daily diet of the pregnant woman will prevent the appearance of any vitamin C deficiency.

RALPH A. REIS.

Gaehtgens and Werner: Vitamin C Deficiency During Pregnancy and Lactation, Klin. Wchnschr. **16**: 843, 1937.

The authors used the Jeszler-Kapp method for determining the vitamin C content during pregnancy and lactation. A marked deficiency of vitamin C was found in 62 per cent of the primiparas and in 70 per cent of the multiparas examined. In those women in whom a vitamin C deficiency was ascertained, tests showed the same general deficiency during the lactation period. Apparently no compensatory rise occurs.

RALPH A. REIS.

Gaehtgens, G.: The Passage of Carotin and Vitamin A From the Maternal to the Fetal Circulation, Arch. f. Gynäk. **164**: 398, 1937.

Comparisons were made of the amount of carotin and vitamin A in the venous blood of 23 women during labor and the content of umbilical cord blood. Vitamin A was never found except in traces and carotin in only very small quantities in the fetal circulation. No definite relation could be ascertained between the quantities in the maternal blood (which always contained larger amounts) and in the fetal blood. The passage of vitamin A and carotin from the maternal circulation to the fetal circulation cannot be entirely explained on simple physicochemical changes. There must be some other regulatory mechanism which permits only certain small amounts to pass through the placenta, first, to prevent a hypervitaminosis of the fetus and, second, to prepare the fetal liver for its post-partum function of storing vitamin A and carotin.

RALPH A. REIS.

Neuweiler, W.: Vitamin C and Placenta, Arch. f. Gynäk. **162**: 384, 1936.

The author was able to demonstrate the presence of vitamin C in the placenta by indophenol titration, by methylene blue, by the ferment method and by animal experimentation. The concentration of vitamin C depends on the method of extraction. The method recommended by Fujita was found to be inaccurate. The tests during early pregnancy gave findings higher than normal, but the author doubts the reliability of such findings. The vitamin C content is somewhat higher on the maternal than on the fetal side of the placenta. The origin of both is the available vitamin C in the maternal blood stream. The vitamin C is apparently stored in the outer layer of the chorionic villi, thus assuring a continuous supply for the fetus.

RALPH A. REIS.

Tonutti and Plate: Vitamin C in the Human Placenta, Arch. f. Gynäk. **164**: 385, 1937.

The authors were able to demonstrate the presence of vitamin C in the human placenta, in the decidual, the syncytial, and in the stroma cells. The decidua maintains a constant level of concentration in the placenta, since the vitamin C passes rapidly through both the syncytium and stroma. An increase in vitamin C intake is immediately evidenced by an increase of the substance in the placenta. In all patients studied there was found a vitamin C deficiency. (This investigation was carried out entirely during the winter months.)

RALPH A. REIS.

Bentivoglio, Franco: Maternal-Fetal Metabolism of Vitamine C, Folia Gynaec. (Genova) **33**: 207, 1936.

The author made quantitative determinations of the amount of ascorbutic acid (vitamin C) in the blood and organs of guinea pigs in various states of gestation and under varying dietary regimes.

The most notable finding was that accumulation of vitamin C in various organs during pregnancy was much less than in the nongravid state. The author believes that there is no overproduction of vitamin C during pregnancy but that there is a liberation of this vitamin into the blood from deposits in the organs.

When the animal is kept on a vitamin free diet the vitamin values are higher in the fetus than in the mother. The author feels that the possibility cannot be excluded that a slight amount of synthesis of vitamin C occurs in the fetus.

MARIO A. CASTALLO.

Gaehtgens, G.: Avitaminosis of Pregnancy as the Result of Intestinal Disease, Klin. Wchnschr. **16**: 445, 1937.

The author reports a case of marked avitaminosis during pregnancy. There was a marked deficiency of vitamin C which the author believes to have been due to an

ulcerative colitis from which the patient was suffering during her pregnancy. This deficiency was corrected by parenteral administration of vitamin. The author discusses the entire problem of avitaminosis and calls attention to the especial danger of this condition arising during pregnancy when there is any co-existent gastro-intestinal disease present. In the presence of such a combination the deficiency must always be corrected.

RALPH A. REIS.

Chatterjee, Sachindra Nath: Role of Diet During Pregnancy With Special Reference to Vitamins, Indian Med. Rec. **55**: 200, 1935.

The diet of the expectant mother should consist of simple nutritious foods, mixed in character, containing fruits, vegetables, rich in mineral and vitamins, as well as milk from healthy cows. The urine should be checked regularly and if albumin is present, the protein foods, eggs, fish, meat and, if need be, milk should be restricted. A well-balanced diet will provide the necessary calcium and phosphorus for mother and fetus. Foods rich in iron and copper must be provided, i.e., spinach, liver, apples, etc. Vitamins are very important in the diet of the pregnant woman. All the vitamins from A to E should be administered. They play a great part in the development of immunity and, therefore, lower morbidity and mortality in mother and infant.

F. L. ADAIR AND S. A. PEARL.

Watson, E. M.: Clinical Experiences With Wheat Germ Oil (Vitamin E), Canad. M. A. J. **34**: 134, 1936.

Watson prescribed wheat germ oil to 65 patients in whom spontaneous abortions, threatened abortions or involuntary sterility constituted the principal abnormalities.

In the majority of the abortion and sterility cases no therapeutic measures except the use of wheat germ oil were instituted. But the patients with signs of threatened abortion furthermore were subjected to the management usual for that condition. Of eleven patients who previously had from 3 to 15 spontaneous abortions, 9 went to term and were delivered of healthy living children. Six of the patients under this regimen completed a pregnancy for the first time. Of the 17 wheat germ oil treated patients, each of whom had had 2 spontaneous abortions, 12 gave birth to healthy living children after the use of the oil. In 5 cases the pregnancies were interrupted by spontaneously occurring abortions. Of 9 treated patients, each of whom had experienced one previous spontaneous abortion, 8 gave birth to healthy, living children. In the ninth, one abortion took place a short time after the use of the oil was commenced. Fifteen patients were treated for the symptoms of threatened abortion, the majority after bleeding had begun. In 11 of these the pregnancies continued uninterruptedly to term, but in 4 the abortion became inevitable. Thirteen nonpregnant women were given wheat germ oil with a view to facilitating impregnation. Six of these had never conceived and therefore constituted examples of primary sterility. Each of the remainder had been pregnant at least once. Seven had had one or more abortions, but only one woman had given birth to a living child. Pregnancy did not ensue in any of the patients in this group. The experiments lend some support to the surmise that vitamine E is a factor in the advancement of pregnancy to a natural termination.

J. P. GREENHILL.

Theobald, G. W.: Effect of Calcium and Vitamins A and D on Incidence of Pregnancy Toxemia, Lancet **1**: 1397, 1937.

This study centered about the possible influence of additional calcium and vitamins A and D on the incidence of toxemia of pregnancy. A series of 100 patients, not more than twenty-four weeks pregnant, were divided into two units of 50, one for the control. The members of the other group were requested to take daily 20 gr. of calcium lactate, 11,000 (international) units vitamin A, and 450 units of vitamin D.

In the group on regular diet, 28 patients showed evidence of toxemia, while only 13 of those taking calcium and vitamins A and D had such symptoms.

These results strongly suggest that a main factor in the prevention of toxemia is the vitamin-B complex. The author recommends that others make similar observations. The writer asserts that the difference between the two groups in this series is too great to be explained by chance.

H. CLOSE HESSELTINE.

Shute, E.: Anti-Proteolytic Properties of Human Blood Serum in Cases of Miscarriage and Premature Labour, J. Obst. & Gynaec. Brit. Emp. **44**: 253, 1937.

The literature dealing with the vitamin deficiencies and the hormonal factors concerned with premature interruption of pregnancy in animals and man is discussed by Shute. A large percentage of patients who miscarry or are prematurely delivered show an excess of estrogenic substance in the blood serum. This produces a resistance in that blood serum to its digestion by such a proteolytic enzyme as trypsin. This resistance to proteolysis temporarily disappears from the maternal blood on administration of an adequate quantity of fresh vitamin E and simultaneously symptoms and signs of impending labor cease. With cessation of vitamin E therapy, this estrogenic substance usually reappears in the blood, and coincidentally symptoms and signs of threatened labor may show themselves again.

J. P. GREENHILL.

Vogt-Moeller: Treatment of Habitual Abortion With Wheat Germ Oil (Vitamin E), Klin. Wchnschr. **15**: 1883, 1936.

Vogt-Moeller reports results obtained in his last 56 cases of habitual abortion. To obtain living children he prescribed vitamin E in the form of wheat germ oil. He was rewarded by delivery of 38 full-term babies.

J. P. GREENHILL.

Dicker, S.: Treatment of Vomiting of Pregnancy by Ascorbic Acid (Vitamin C), Schweiz. med. Wchnschr. **67**: 74, 1937.

Eight cases of severe hyperemesis gravidarum were treated with vitamin C by Dicker. In all the cases there was a sudden cessation of symptoms or at least a decided and progressive improvement. The author administered vitamin C by the intravenous route. The favorable action is due to restoration of the thyroid-vitamin C equilibrium.

J. P. GREENHILL.

Brehm: Potential Dangers of Viosterol During Pregnancy: With Observations of Calcification of Placenta, Ohio State M. J. **33**: 990, 1937.

Some obstetric patients need more calcium and vitamins than provided by a normal diet. In the opinion of Brehm viosterol causes definite calcification in the placenta, which is greatly increased by the ingestion of calcium. Viosterol may also be responsible for calcification in the kidney of the newborn. Cod liver oil seems preferable to viosterol or irradiated ergosterol. Natural vitamins, when indicated, seem preferable to synthetic products. It is important in treating a patient not to produce by overtreatment a more serious condition than the one originally treated. Considerably more research is required before the promiscuous use of viosterol during pregnancy can be continued.

J. P. GREENHILL.

Items

American Board of Obstetrics and Gynecology

The oral, clinical, and pathological examinations for Group A and Group B applicants will be held in San Francisco, California, on Monday and Tuesday, June 13 and 14, 1938.

An informal dinner for the Diplomates of this Board, their wives and others interested in the work of the Board, will be held at the Palace Hotel, San Francisco, on Wednesday evening, June 15, 1938, at seven o'clock. Dr. William D. Cutter, Secretary of the Council on Medical Education and Hospitals of the American Medical Association, will address the group, and the successful candidates of the preceding two days' examinations will be introduced in person. Tickets, at $2.25 each, may be obtained in advance from Dr. Joseph L. Baer, 104 S. Michigan Avenue, Chicago, Illinois, or at the door. Reservations should be made in advance if possible.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

American Committee on Maternal Welfare

A meeting of members and directors is called for Thursday, June 16, 1938, at 6:30 P.M., at the Palace Hotel, San Francisco, Calif., for the purpose of electing directors and for the transaction of other business which may be presented.

Also there will be an open luncheon meeting of the Committee on Maternal Welfare, on Wednesday, June 15, 1938, at 12 noon, in the Borgia Room, St. Francis Hotel. This is to be followed by a business meeting at which will be discussed the program of the forthcoming American Congress on Obstetrics and Gynecology to be held in Cleveland, Ohio, September 11 to 15, 1939.

All those interested are invited to attend. For further information address the Headquarters office, 650 Rush Street, Chicago, Ill.